SURGERY, GYNECOLOGY AND OBSTETRICS

AN INTERNATIONAL MAGAZINE, PUBLISHED MONTHLY

VOLUME XIX NOVEMBER, 1914 NUMBER 5

THE CHOICE OF THE METHOD OF OPERATION IN THE TREATMENT OF GASTRIC AND DUODENAL ULCER

WITH A REVIEW OF MY EXPERIENCE ACCUMULATED IN THE PAST TEN YEARS[1]

BY PROFESSOR FREIHERR A. VON EISELSBERG, VIENNA, AUSTRIA

IN spite of the progress made in the diagnostics of gastro-intestinal diseases, among which I place röntgen examination first, the choice of the method of operation for gastric ulcer and its complications can best be made at autopsy *in vivo* when the abdominal cavity is opened. It is most important that the operator should satisfy himself whether there exists an ulcer with an unhealed surface or a healed ulcer, in fact a scar, and whether the ulcer is situated at the pylorus or at a distance from it. When in possession of these facts he is in a position to decide which operation is to be recommended: gastro-enterostomy only, pyloric exclusion, or as a last resort, resection.

The operations for the acute and chronic conditions found in gastric ulcer are among the finest achievements in modern surgery. That the operation is a gratifying one and justly fills the surgeon with pride and satisfaction will be admitted by all who have witnessed the recovery of a patient who had been suffering from an acute perforation due to a gastric ulcer and who has been rescued from imminent peril, by laparotomy, irrigation of the peritoneal cavity, and suture of the ulcer; or, again, the restoration of a patient suffering from chronic pyloric stricture to perfect health, by gastro-enterostomy.

Gastro-enterostomy, especially, has come to be considered the operation most frequently attended with beneficial results, and to-day there is no operation so often done in the gastro-intestinal canal, excepting of course appendix resection. Where the operation can be performed it is now recognized as the universal method of treatment in all cases of ulcerated processes of the stomach. But the happy results of gastroenterostomy just now mentioned are not evident in all cases. In cases of persistent ulcer particularly, its cures are not so numerous as in the cases of ulcers already healed. In cases where the ulceration is at a distance from the pylorus, the result of gastro-enterostomy is not so good as in cases where the ulceration is situated *at* the pylorus. Especially to my former pupil, Professor Clairmont, is due the credit of having discovered this. And finally, one must always bear in mind that there may be a possibility of carcinoma in cases of tumor formation and obviously in these cases removal only is efficient, while a gastro-enterostomy would have, at most, a palliative value.

In consideration of the fact that gastro-enterostomy has become the usual operation in the treatment of gastric ulcers it behooves us to look very carefully into its merits. My deductions will be directed particularly to the

[1] Read before the Clinical Congress of Surgeons, London, July 27, 1914.

question of the value of gastro-enterostomy as compared with other operations for gastric ulcers, and I will define especially the conditions which indicate resection of the stomach.

While I review my cases of gastric ulcers, I would direct your attention to Table I which summarizes the gastro-enterostomies for ulcerative processes performed in my clinic during the past ten years. My former pupil, Professor Clairmont, has helped me very considerably in collecting and arranging this great mass of material. He will shortly publish a large work dealing with our combined experiences in the operative treatment of gastric ulcer.

Now, if we look at the Table I we shall see that out of a total of 334 gastro-enterostomies for gastric ulcer, seventeen died after the operation. In twelve of these the ulcer was recent. Eight died from causes referable to the ulcer itself; for instance, hæmorrhage from the ulcer, progressive ulceration. Thus it will be seen that gastro-enterostomy in some cases not only did not stop the hæmorrhage, but apparently induced it.

Now, let us turn to the heading "recoveries," which shows the results estimated after a considerable interval. Under "cured" we include those cases in which the patient is fully relieved from every symptom and inconvenience and is in proper condition to continue his calling. If any trouble or pain remained, however small, the patient is shown under the heading "improved."

The data listed under "unrelieved" and "died at a later period" are especially interesting. In eight of the thirty-one "unrelieved" cases, the ulcer was situated at the pylorus. In eleven cases the ulcer was situated at a distance from the pylorus. Eight cases were duodenal ulcers. In four cases the ulcer was not located; there were adhesions and probably the ulcers were duodenal.

The interesting point demonstrated by these thirty-one cases is that ulcers situated at a distance from the pylorus, "*pylorusfern*," are not so greatly influenced by gastro-enterostomy as those situated at the pylorus. First among the causes which are responsible for failure to cure by operation is the development of a post-operative peptic ulcer of the jejunum. This occurred seven times in 334 gastro-enterostomies. Of this formidable complication after gastro-enterostomy I will speak fully later on.

Finally, with regard to the cases shown under the heading "died at a later period," in only a limited number are the causes of death known.

Thirteen patients, or about ten per cent, died of cancer of the stomach. In six the continuance of the growth and the development of the ulcer after the operation were the causes of death. In one of these six cases, the patient developed the morphine habit through the pain he suffered, and died; another died from hæmorrhage; another died following perforation of the ulcer; another had very severe pain and hæmorrhage: jejunostomy was performed, but the patient committed suicide; and finally in one case the pains con-

TABLE I

GASTRO-ENTEROSTOMY FOR ULCER OF THE STOMACH AND DUODENUM

	Cases
Total number of cases	334
1. Death after operation, 5% (ulcer recent in 12)	17
Causes of death:	
Hæmorrhage from ulcer	5
Anæmia following repeated attacks of hæmorrhage	2
Progressive course of ulcer	1
"Circulus vitiosus"	2
Failure of heart action (4 weeks later)	3
Peritonitis	1
Pneumonia	1
Paratyphoid	1
Enteritis and marasmus	1
2. Recoveries	317
Number of cases operated in 1913	48
Number of cases operated previous to 1913 (107 recent ulcers)	269
Cured (recent ulcers in 49)	134
Improved (recent ulcers in 24)	42
Lost sight of	21
Unrelieved (recent ulcers in 15, 7 developed post-operative peptic ulcer)	31
Ulcer at pylorus in	8
Ulcer at varying distances from pylorus	11
Duodenal ulcer	8
Ulcer not definitely located, probably in duodenum	4
Number of cases who died at a later date (recent ulcers in 19)	41
Cause of death known in only	23
Cancer of the stomach	13
Extension of disease[1]	6
Tuberculosis of the lung	3
New-growth of the kidney	1

[1] One patient became a morphomaniac and died. One died from hæmorrhage. One from perforation. On one a jejunostomy was performed for severe pain and repeated hæmorrhage, and he finally committed suicide. In one there was constant pain.

tinued but further details are unknown. Three patients died of tuberculosis of the lungs. One patient died of tumor of the suprarenal body. The cause of death in the remainder is unknown.

We see, therefore, that of forty-one patients who died, most of them years after the operation of gastro-enterostomy, thirteen—that is, nearly one-third of the number—were victims of carcinoma, while six succumbed to the continued extension of the symptoms due to the ulcer.

In thirty-six cases of ulcerative processes in the stomach and duodenum, unilateral pyloric exclusion was performed. In some instances this operation was done in the cases of still ulcerated and bleeding ulcers in the neighborhood of the pylorus and in some instances in cases of ulcers localized in the duodenum. Pyloric exclusion appears to be especially suitable in the latter case.

Table II summarizes the results of unilateral exclusion of the pylorus with gastro-enterostomy of the stomach and duodenum. Twelve operations were performed during 1913, but the interval after operation is too short to make a definite statement regarding results. However, we may state that eleven patients made a complete recovery after the operation, and some of the cases were operated upon in the years 1905 and 1906. Under "improved" we have even included cases complaining of insignificant symptoms, and nearly all of them might justly be shown under the heading "cured." Of the four cases under "unrelieved" we note that in one the whole ulcer was extirpated to relieve the continued pain, and cure followed; one patient still suffers from attacks of hæmorrhage; and two patients developed symptoms of peptic ulcers. Of three cases who died at a later date, one case developed cancer of the stomach and two patients developed peptic ulcers.

TABLE II

UNILATERAL EXCLUSION OF THE PYLORUS WITH GASTRO-ENTEROSTOMY OF THE STOMACH AND DUODENUM

Total number of cases	36
Mortality after operation	0
Subsequent Results:[1]	
Number of cases cured	11
Patients lost sight of	1
Improved	5
Unrelieved	4
On one patient a second operation (resection of the whole ulcer) was successfully performed and the patient relieved entirely of symptoms.	
One patient suffers repeated attacks of hæmorrhage.	
Two patients developed, later, symptoms of a post-operative peptic ulcer, but no further operation was performed.	
Death at later date	3
One patient died of carcinoma of stomach; two developed post-operative peptic ulcer.	

[1] Twelve operations were performed during the year 1913, so the interval is not sufficient for a definitive statement as to results, but up to the present are apparently cured.

SOME REMARKS ON PEPTIC ULCER

As the topic of the development of peptic ulcer again occurs at this point, I should like to go into the subject more in detail, especially as it seems to me that the facts concerning peptic ulcer of the jejunum are not so generally known as they should be.

As has already been pointed out by H. Braun of Göttingen, the discoverer of this serious complication following gastro-enterostomy, peptic ulcer appears to be caused by the continuous passage of the acid gastric juice into the small intestine, the duodenum, causing erosion of the mucous membrane and giving rise to the growth of an ulcer. The lesion seems to occur in varying intensities. In the less severe cases symptoms in the form of simple pains such as an ulcer usually causes, may occur. In such cases, as in all ulcerative processes, repair on the part of the organism may bring about a cure; and in the cases of spontaneous cure, contraction and stricture of the gastro-enterostomy wound-area seem to take place very easily. I cannot explain in any other way my observations in two instances, once in Königsberg and once in Vienna; namely, the *shrinking* of a gastro-enterostomy fistula, which I had made of normal size, to one-third its size without any appreciative induration. Kehr described years ago the spontaneous closure of a gastro-enterostomy fistula and I presume the closure was caused by the healing of a peptic ulcer; for I believe that all these contractions are effected by the healing of a not very intensive peptic ulcer, thereby closing the fistula.

In other cases the ulcer itself spreads, and with the serious and tragic issues of this condition we have to deal briefly to-day.

TABLE III

POST-OPERATIVE PEPTIC ULCER[1]

Methods and Results of the Further Operations

	Cured	Improved	Lost sight of	Unrelieved	Died
Gastro-enterostomy, 6 cases		One case seen nine months after operation	2	1	One died from post-operative peritonitis. One died from a later relapse of the ulcer.
Gastro-enterostomy and later jejunostomy		One, seen one year after operation			
Jejunostomy and later gastro-enterostomy				1	
Jejunostomy	1				
Gastro-enterostomy and jejunostomy at the same time					1
Gastro-enterostomy and later resection of the ulcer		One			1
Excision and gastro-enterostomy at same time		One, seen one year after operation	1		1
Total	1	4	3	2	5

[1] In fifteen cases diagnosed as post-operative peptic ulcer, a further operation was performed and the diagnosis confirmed. Ten patients had been operated the first time in my clinic (gastro-enterostomy, 7 times; exclusion of pylorus, 3 times); on five patients the first operation was performed elsewhere.

I have observed the formation of peptic ulcers seven times in gastro-enterostomies. In addition to this I have found peptic ulcers in five patients on whom gastro-enterostomies had been done by other surgeons and in one on whom I myself did re-laparotomies. Thus in each of the twelve patients a peptic ulcer was verified at the autopsy *in vivo*. Finally there were four patients who developed symptoms of peptic ulcer following unilateral pyloric exclusion. In the seventeen cases the chief symptom was the development of a very painful induration in the neighborhood of the gastro-enterostomy fistula, the discomfort and pain becoming so great that one could scarcely touch the spot. In fifteen of the cases, the diagnosis of peptic ulcer was verified by subsequent re-laparotomy. Two patients were not operated on. Gastro-enterostomy, jejunostomy, or finally an excision of the whole ulcer, was done at the re-laparotomies and in some cases more than one of these operations was done, either at one operation or in several.

Table III shows the cases in which peptic ulcer developed. In six patients a fresh gastro-enterostomy was done at the re-laparotomy, but otherwise the ulcer itself was not touched. Only one of the patients was substantially improved after an interval of nine months; one was not relieved; one was lost sight of; two died, one of the two fatal cases dying immediately after the operation from peritonitis and the other later from relapse of the ulcer. In one patient, as the gastro-enterostomy did not bring the hoped-for relief, jejunostomy was done in addition, and although by this measure the stomach was entirely placed out of action, a very marked improvement followed which has now been maintained for nine months. In a later patient the operations were carried out in the reverse order: first, a jejunostomy and later a gastro-enterostomy; and I wish to call your attention to the history of this case:

The patient had hæmorrhages pointing to duodenal ulcer with a high general acidity of 77 and free hydrochloric acid, 66, compared with the normal, 60 to 45. The laparotomy July 27, 1912, disclosed an ulcer in the duodenum, for which unilateral pyloric exclusion was done. After this operation the acidity did not diminish, at least not so much as is usual, and hæmorrhage recommenced. Therefore on October 14, 1912, another laparotomy was done and a very large peptic ulcer was found, which seemed to be non-operable. A jejunostomy was now done and a completely satisfactory improvement followed. The patient believed himself now quite recovered and urgently requested that he be allowed to dispense with the catheter. Unfortunately, we yielded to the very strongly expressed wish. Alas! All too soon. The catheter was taken out, and on January 27, 1913, the fistula had spontaneously closed. In three months severe pain returned and melæna appeared. Again on April 23, 1913, laparotomy was done and the peptic ulcer was found in as bad a state as it was before. It did not seem now that the ulcer could be removed and a gastro-enterostomy antecolica anterior plus entero-anastomosis was done. After this there was improvement but not for long, for at the beginning of 1914 the patient returned to the clinic with all the symptoms of a gastrocolic fistula. He would not consent to further operative treatment. As before the gastric acidity was very high and the patient appeared to me to be beyond help. This man had too great an amount of hydrochloric acid and the jejunostomy should not have been dispensed with

so soon. Perhaps one could still treat him successfully with Azymon (Magnes chlorata Glaessner).

In a female patient we obtained a favorable result with jejunostomy alone. A girl 27 years of age (who in her seventh year had been successfully operated on by Billroth for hydatid of the liver) had had pains in the stomach for two years and the typical symptoms of stenosis of the stomach. On the 7th of June, 1910, gastro-enterostomy retrocolica posterior was done. Soon after the commencement of a good recovery there developed in the abdomen a hard tumor attached to the anterior abdominal wall. Suspecting a peptic ulcer, laparotomy was done and the suspicion confirmed. Because of the extension of the tumor and the fact that it was intimately connected with surrounding parts, a jejunostomy only was possible, August 8, 1912. This was done nearly three months after the first operation. For three years the patient was given all her food through the fistula and the tumor disappeared entirely so that she could be fed from above thus allowing the fistula to close. The simple removal of the catheter was sufficient and the patient has been entirely cured for two years. *This case illustrates the success of jejunostomy.*

In another patient gastro-enterostomy and jejunostomy were done at the same time. This patient had been operated on September 9, 1909, for a very high general acidity combined with an unhealed ulcer which extended into the duodenum. A unilateral pyloric exclusion was done. After a short time the pains commenced again and the patient was re-laparotomized on January 22, 1910, and a peptic ulcer found situated at the site of the gastro-enterostomy. Therefore a new gastro-enterostomy antecolica anterior plus entero-anastomosis and lastly, on account of the high acidity, a jejunostomy as well, were done. The patient died with symptoms of hæmatemesis. At the post-mortem five recent ulcers were found distal to the jejunal stump; one of the ulcers was on the point of perforating. At the site of the old gastro-enterostomy was an annular ulcer which appeared to be turning into a gastrocolic fistula.

In two cases gastro-enterostomy and then resection of peptic ulcer were done.

One patient had to be operated on three times. First, a resection, later a new gastro-enterostomy antecolica anterior plus entero-anastomosis were done. Relief followed for one month; then gastric trouble occurred again, and there developed a painful tumor in the neighborhood of the stomach. On June 10, 1913, laparotomy was performed, the peptic ulcer resected widely, the incisions passing through the quite normal tissue, and a fresh gastro-enterostomy antecolica anterior plus entero-anastomosis done. An improvement followed lasting only a short time when stomach trouble again set in and on November 31, 1913, the patient died with symptoms of a gastrocolic fistula.

Finally, in three cases resection of the whole ulcer was performed and of course, at the same time, a fresh gastro-enterostomy fistula was established. This was necessary because we could not make a direct suture of the wound of the fistula.

In the first patient we did a new gastro-enterostomy plus entero-anastomosis after resection of the peptic ulcer, whereupon there was improvement at last. The second patient was lost sight of and the subsequent history is not known. One patient died after resection.

These facts show that the growth of a peptic ulcer of the jejunum presents a very serious complication; even repeated operations, employing very severe measures, are useless and patients have finally succumbed to the peptic ulcer. Other authors, among whom I would mention Haberer of the Insbruck Clinic, have also spoken of the gravity of this same complication in which repeated radical measures are necessary.

If we inquire into the causes of these ulcers, the high hydrochloric acid value of the gastric juice must be mentioned before all others. In some cases the patient had vascular disease, either an arteritis, an endarteritis, or a periarteritis.

I have observed this formidable complication in a surprisingly large number of cases and I cannot tell why I should have met with peptic ulcers more frequently than other surgeons. I should not like to say how much technique has to do with it. Peptic ulcers appear to me to be more frequent during the last years and I am inclined to attribute their frequency to the fact that open or unhealed ulcers are operated on more frequently than formerly.

It may be that many peptic ulcers which are known to cause extensive tumor formation and severe symptoms have led surgeons to think that cancer was present and so the question of further operations has been laid aside. Great care in the after-treatment of cases may possibly go far in the prevention of the development of peptic ulcers. For a peptic ulcer which has already manifested itself, a total excision is the best treatment.

A short time ago I operated on just such a case, the primary gastro-enterostomy having been per-

formed by another surgeon. It was an exceptionally difficult case, as the whole peptic ulcer together with the loop was excised. I made the blind suture of both openings of the jejunum and then implanted the distal stump into the stomach and the proximal one into the distal. So far the progress of the cure has been rather satisfactory.

TABLE IV

RESECTION FOR ULCER OF THE STOMACH

Immediate results of the Operation			Subsequent Results			
	Cured	Died	Cured	First Improved, Later Relapsed	Unrelieved	Died
Female	36	4	26	2	1	2
Male	20	5	15	0	1	0
Total	56	9[1]	41[2]	2	2	2

[1] Of the 9 cases which succumbed to operation, (a) six died from peritonitis; four, from the leakage of the stomach content; one, from leakage through duodenal stump; and one from chronic peritonitis; (b) one died from hæmorrhage from an ulcer which formed after the operation; (c) one died from perforation of a new ulcer; (d) one died from a stricture of the gastroduodenal suture, forty-eight days after the operation.

[2] Of these, nine were operated upon in the year 1913, and the interval is too short to estimate results.

What I wish to emphasize is, that whenever possible the peptic ulcer should be excised, for I have found in my experience that neither gastro-enterostomy nor jejunostomy are sufficient in themselves, and in many cases both operations combined are of no avail. We have already mentioned among the cases of post-operative peptic ulcer, five patients on whom the first gastro-enterostomy was performed by other surgeons. I am therefore somewhat skeptical when I hear surgeons state that they have never met with a peptic ulcer.

In Table IV, I have summarized the cases in which the ulcer was excised. In the nine cases of death after operation, the following proved to be the causes: In six cases post-operative peritonitis, caused by leakage of gastric juice[1] in four; by leakage of the duodenal stump in one; and in one by chronic peritonitis. In one case pyloric resection after Billroth's method No. 2 was done. The ulcer recurred and led to a fatal hæmorrhage. The total acidity was enormously high, 104, and even resection did not prevent the repeated formation of ulcers. This patient had a very strong tendency to the development of peptic ulcer.

[1] In spite of the strongly acid gastric juice the discharge from the ulcer is often highly infected; it has repeatedly been shown to contain streptococci.

In one case the patient died later from the formation of a new ulcer which perforated. In one case the patient died 48 days after an operation by Billroth's method No. 1. He developed a secondary stenosis of the gastroduodenal suture and died. In this case a gastro-enterostomy might easily have been helpful.

RESULTS OF RESECTION

The forty-one cases shown as cured are all quite well, but nine of them were operated on only last year.

Under "first improved, afterwards relapsed," we have only one case in which an excision of the ulcer and at the same time a gastro-enterostomy retrocolica posterior was performed, and one case in which a resection by Billroth's method No. 2 was done.

Under "unrelieved" we have two cases. In the first case a wedge-shaped excision of the ulcer was made and this was followed by stenosis at the site of the excision. Gastro-enterostomy antecolica anterior plus entero-anastomosis was performed and since this operation the patient is cured. This is direct evidence against the method of excision of the ulcer, and the operation should be replaced by resection. Whether in this case the repeated formation of the ulcer was traceable to a process analogous to the formation of a peptic ulcer must be left undecided. Wedge-shaped resection can easily lead to a sharp kinking of the vessels and so may lead to a disturbance in the circulation and its resulting consequences (such as cicatrices — perforations).

In the second case resection by Billroth's method No. 2 was performed in 1911. The patient had a recurrence of the trouble.

Under "died" we have two cases: one dying after three years from stomach trouble, probably carcinoma; one, after three years and two months, from cancer.

SUBSEQUENT RESULTS OF RESECTIONS WITH REFERENCE TO THE METHOD OF OPERATION

Table V shows good results. Forty-one cases were cured. In one case of improvement followed by relapse, resection by Billroth's

method No. 2, it should be noted that the patient was well for one and one-half years and then began to suffer pain in the left side. The single case of excision which was not cured had a second laparotomy performed on account of recurring trouble. In spite of a wedge-shaped resection a stenosis of the stomach had developed.

TABLE V
SUBSEQUENT RESULTS OF RESECTION
With Reference to Method of Operation

Operation	Cured	First Improved, Later Relapsed	Died
Transverse resection of stomach	12		
Billroth II	27[1]	2	1
Excision plus gastro-enterostomy	1	1	
Excision alone	1	1	1
Total	41	4	2

[1] Of these, eight were operated on in the year 1913.

Finally, in a series of cases jejunostomy alone was performed. We need not wonder at the high mortality of the operation, as it was performed in the weakest and the worst cases, when the conditions were so complicated that nothing else was possible or where the patients were so weak and worn out that one could only do the shortest operation possible under local anæsthesia.

There were twenty-four cases with twelve deaths, and eight of these died of peritonitis; one of hæmorrhage from the ulcer—in other words, hæmorrhage in spite of the jejunostomy; one from tubercular complications; one from degeneration of the heart muscle and one of marasmus. Twelve cases survived the operation; but two died later, both of carcinoma. One case was improved, four cases were lost sight of, and five cases were completely cured.

On the basis of our observations we are able to lay down the following rules for the choice of method of operation.

1. For acute perforation the best method is immediate laparotomy with irrigation of the peritoneal cavity and closure of the orifice of the perforation. Whether gastro-enterostomy should be done afterward depends on the situation of the ulcer and the general condition of the patient. If the patient is so weak that a gastro-enterostomy is out of the question, and can eat nothing on account of the peritonitis being already far advanced, then jejunostomy is the simplest operation, as it makes it possible to feed the patient immediately after the operation.

2. I will remark here that in the other complication of ulcer which we fear so much, namely, hæmorrhage, it is better not to operate. When the hæmorrhage is severe, expectant treatment is the best, for it has repeatedly occurred at the operation that the bleeding point could not be found. This is one of the most hopeless situations in which a surgeon may find himself, for the patient may die during the operation. On the other hand, it is surprising how much blood a patient may lose without dying. One can stop a good deal of hæmorrhage with rest in bed, ice bags to stomach, injections of gelatine, serum of horses, the administration of calcium lacticum. In hopeless cases we can make a trial of strong silver nitrate, 1 in 100 solution, for irrigation. In extreme cases, jejunostomy should be performed, as one can give the stomach absolute rest and at the same time give the patient nourishment. If the hæmorrhage is severe but has stopped for the time being, one should operate at once before the hæmorrhage recommences.

3. In typical stenosis of the pylorus, especially in the case of a long-standing ulcer where no new symptoms have occurred, gastro-enterostomy is the operation to be selected. Sixty per cent of the cases of stricture of the pylorus are completely cured by gastro-enterostomy while in the cases of open ulcer gastro-enterostomy is successful in only 41 per cent of cases. Among 334 gastro-enterostomies for ulcer of the stomach and duodenum and its complications, seventeen deaths occurred. Of these, eight (nearly one-half) were caused by continued bleeding from the ulcer. Therefore, gastro-enterostomy is not in all cases a complete protection against continuance of the hæmorrhage.

4. Unilateral pyloric exclusion (which I did first in 1894) offers the greatest security in dealing with ulcer and its complications. It should receive special consideration in cases

in which the ulcer is still fresh and causing much pain and finally in cases of duodenal ulcer. It seems to offer the best guarantee of stopping hæmorrhage even though this guarantee is not a positive one.

5. For ulcer situated at a distance from the pylorus simple gastro-enterostomy is not so feasible as in cases of ulcer of the pylorus itself. Professor Clairmont was the first to show this from evidence collected at our clinic. It offers only 34 per cent of successes as contrasted with 54 per cent successful cases of pyloric ulcer. Perhaps this can be partially explained in that an ulcer situated away from the pylorus produces fewer symptoms than one at the pylorus, and is therefore not recognized so soon and is not operated on till much later and in a far more advanced condition.

6. High hydrochloric acid values of the gastric juice, by distinctly favoring the development of post-operative peptic ulcer, detract much from the value of gastro-enterostomy and exclusion. Whether, as it really seems, post-operative peptic ulcer appears more readily after pyloric exclusion is not yet certain. We have done pyloric exclusion especially in the cases of duodenal ulcer, when an ulcer appeared spontaneously in the small intestine, so that the small intestine already seemed predisposed to the formation of an ulcer.

7. I have seen this post-operative peptic ulcer after operations performed by myself and my assistants in the hospital, and I have seen it as well in patients who had been operated on by other surgeons, so that the growth of such an ulcer cannot be attributed alone to our perhaps faulty technique. The danger of the formation of a peptic ulcer is especially apparent in such cases where gastro-enterostomy was not strictly indicated. There are cases in which the history of the patient given by himself points to a gastric ulcer but in which the signs of gastric ulcer are wanting at the laparotomy. There may perhaps be merely a relatively small stenosis of the pylorus, some adhesions or cicatricial tissue in the stomach. In former years it was more easy to decide on gastro-enterostomy in such cases. One regarded it as a safety valve and also a prophylactic precaution against a stenosis that might occur later, and leave the patient in a more serious condition. It is certainly an advantage to remove the appendix at the time of any abdominal operation if it can be done easily. At the same time a gastro-enterostomy should be performed only when there are special indications and not in cases where the stomach symptoms are not severe, perhaps depending solely on the history given by the patient. Since H. Braun made us familiar with the serious complication of post-operative peptic ulcer of the jejunum great care is necessary with reference to it.

In cases when by autopsy *in vivo* I have found no tangible condition to indicate what one had expected to find, judging from the history of the case, and when I have found nothing to show what sort of an ulcer it was, I have simply done an exploratory laparotomy and have refrained from doing what we may term a "concession gastro-enterostomy."

Among fifteen cases of post-operative peptic ulcers of the jejunum which I have seen following gastro-enterostomies, some performed in my own clinic and some by other surgeons, a whole series of measures, some of them very complicated, were tried to reproduce normal conditions. Only one patient was cured, four improved, three were unknown, two were unrelieved, five died. So we see that peptic ulcer presents a very serious complication.

8. In cases of ulcer situated at a distance from the pylorus as well as in cases where there is a high hydrochloric acid value, *transverse resection* seems to me the operation of choice, as this of all other resections, as for instance extirpation methods, gives the best security against subsequent complications. It must be done wherever there is the least suspicion that the tumor under consideration may be of a malignant nature. Of 269 patients on which gastro-enterostomy was performed in my clinic and who could be kept under observation for some time after, forty-one died at a later stage; thirteen from carcinoma, while six died with continuance of the symptoms of the ulcer. These later deaths speak decidedly in favor of the radical operation. Transverse stomach resection is also the correct operation when the ulcer has invaded neighboring

organs, as nothing except removal of the ulcer will be of any real assistance. Transverse resection as planned by Riedel, also warmly advocated by Payr and Küttner, is a relatively safe operation. Up to January, 1914, we had performed twelve transverse resections to which six more cases may be added up to July 1, 1914, making eighteen in all; and there has not been a single death. I have never seen a peptic ulcer or any other harmful result after this operation.

When transverse resection cannot be done Billroth's method No. 2 should be employed. Billroth's method No. 1 is the third choiçe. Partial excision is to be rejected entirely.

Only in extreme cases, when other operations are not feasible, jejunostomy may be considered, as has already been suggested in cases of perforated ulcer when the patient is so weak that he must be fed immediately after the operation. Jejunostomy makes it possible for nourishment to be given even on the operating table. Further, in cases of peptic ulcer in which for exceptional reasons excision is not possible, it is the easiest and most rapid of all operations for gastric ulcer, and above all it leaves the stomach undisturbed. As it has been done only in extreme cases one cannot wonder that it has met with so little success and that noticeably so many cases of peritonitis have been associated with it. There were patients whose peritoneum had lost its power of resistance.

A FEW REMARKS ON THE TECHNIQUE OF THE OPERATIONS UNDER DISCUSSION

In my clinic gastro-enterostomy is done whenever possible after the method of Hacker, retrocolica posterior with a quite short loop; or better said, without any length of bowel between the stomach and jejunum. The transverse mesocolon is found and an aperture is made in a part comparatively free from blood-vessels. Through this opening the stomach wall is pulled forward and then secured with a Doyen's clamp at a place which is as near as possible to the greater curvature. The small intestine at the junction of the duodenum and jejunum is brought to this spot and sutured. I will not go into a detailed description of the suturing. It is done in the typical way after Wölfler's method: First, inner seromuscular suture; second, inner mucous suture; third, outer mucous suture; fourth, outer seromuscular suture; and then a few Lembert sutures added. It appears to me of especial importance that the slit in the mesocolon should be properly sutured.

In Königsberg I once had an opportunity of observing a case of ileus in which a mesocolon slit made during a laparotomy was left unsutured by my predecessor in the professional chair. This led to an internal strangulation. Since this experience I have always been especially careful in suturing the slit. Finally, a short time ago we had a bad case in our clinic, in which after a gastro-enterostomy the suture which secured the slit to the stomach gave way and led to an internal strangulation.

THE TECHNIQUE OF PYLORIC EXCLUSION

The stomach is divided between two Kocher clamps by a Paquelin cautery, and both proximal and distal ends are sewn by a continuous suture while the clamps are on. After removal of the clamps a further suture beyond the first one is put in for safety. I lay very great stress on the importance of the fact that in unilateral exclusion the nerves of the stump may be severed. This happens only when they are cut through and not when simply a band or fold of fascia is laid around.

THE TECHNIQUE OF TRANSVERSE RESECTION OF THE STOMACH

One is always astonished how far the two cut ends of the stomach retract after removal of the central portion, and he fears that the transverse suture will not be possible. However, it is easier than one would think. It is necessary when doing this operation to supplement the longitudinal incision in the abdominal wall with a transverse incision in order to get plenty of room.

THE TECHNIQUE OF JEJUNOSTOMY

This is especially simple and the method has not changed since I described it in 1894. It is merely adopting the principle of Witzel, substituting jejunum for stomach. I would emphasize especially this point, that the catheter should not be introduced into the intestine at any point lying higher in the abdomen than the umbilicus; otherwise it may lead to a kinking of the intestinal loop.

CONTRIBUTION TO THE DISCUSSION ON THE CHOICE OF OPERATION IN CHRONIC GASTRIC AND DUODENAL ULCERS[1]

By JAMES SHERREN, F. R. C. S., London, England

THE operation to be performed in any individual case of chronic gastric ulcer can be decided only after the abdomen is opened. General rules, however can, be laid down from a study of the post-operative progress of a series of patients treated by individual surgeons by varying methods.

My contribution to this discussion is based upon a personal operative experience of 200 cases of chronic gastric ulcer (*vide* Appendix A) and 224 cases of chronic duodenal ulcer. These figures include only those in which an unhealed chronic ulcer was present, and exclude operations for acute perforation of both acute and chronic ulcers and those in which scarring had produced symptoms, the ulcer being healed.

There is good ground for belief that ulcers of the stomach and duodenum are associated with, and secondary to, disease in and around other viscera, particularly the appendix. It is therefore clear that the whole abdomen should be thoroughly examined and in most cases the appendix removed, except when the patient is seriously ill from hæmorrhage or perforation. In my earlier cases I neglected this and have since had to operate for the removal of gall-stones and chronic appendices overlooked at the original operation.

The treatment of chronic duodenal ulcer consists in infolding the ulcer when it is in its usual situation on the anterior wall and performing posterior gastrojejunostomy.

In my series there were four deaths, all in men over 60 years of age: three from bronchopnuemonia, and one from acute œdema of lungs 24 hours after operation.

The results of gastrojejunostomy in this condition are in my experience unequaled by any other operation.

A hundred of the cases have now been operated upon more than two years. The operative death rate was two. Three have since died from other causes, six, five, and three years after operation, remaining quite well. One died a few months later after prostatectomy. Eighty-five have remained in perfect health.

Two developed jejunal ulcers after eleven and six months respectively. Operation was successfully carried out two and one-half years ago and fifteen months ago, both patients remaining in perfect health. In the whole series I have had to operate upon five, without a death.

Three patients complain of occasional discomfort but are much better. The remainder I have been unable to trace.

A result such as this in my opinion establishes gastrojejunostomy as the operation of choice in cases of chronic duodenal ulcer.

Acute perforation of a chronic duodenal ulcer is by no means an infrequent complication and should be treated by closure or excision followed by gastrojejunostomy.

I have been able to carry out this treatment in fifteen cases with one death, a patient who was suffering also from genito-urinary and pulmonary tuberculosis.

I consider gastrojejunostomy an essential part of the treatment and always carry it out except in the "too-late" cases. In all the survivors in whom this was not done I have since had to carry it out, and have also operated upon five cases in which perforations were closed by other surgeons.

I have entirely abandoned irrigation of the peritoneal cavity, and instead gently sponge away any exudate, close the operative wound, and drain through separate incision when necessary.

All surgeons who have had a wide experience of the treatment of gastric ulcer have found that gastrojejunostomy fails to bring about healing in certain cases, and that relapse occurs in many of those operated upon by excision alone.

Some state that while gastrojejunostomy is a satisfactory procedure in cases of chronic ulcer producing pyloric obstruction, it has not been successful when the ulcer is situated elsewhere. Such, however, is not my experience (*vide* Appendix B). Simple chronic

[1] Presented in the discussion of Professor von Eiselsberg's paper read before the Clinical Congress of Surgeons of North America, London, July 27, 1914. (See p. 555.)

gastric ulcers, wherever situated, will heal as the result of gastrojejunostomy correctly performed unless they are adherent and have perforated, their floor being formed by pancreas or liver, thus preventing the contraction necessary to sound healing.

I am convinced that gastrojejunostomy alone so modifies gastric conditions that ulcers heal, and that only when complications have arisen is excision or partial gastrectomy necessary.

I have had the opportunity of proving this in six of my series in whom chronic ulcers situated on the lesser curvature had been treated by gastrojejunostomy alone. In three cases I had to operate again for causes unconnected with the ulcer or original operation, and in three was able to examine the stomach after death from other causes more than two years after operation. In all, the ulcer had perfectly healed.

Although gastrojejunostomy alone is curative in the majority of cases, it should not become the sole routine procedure. My present practice is to perform gastrojejunostomy in every case, the posterior vertical no-loop operation by preference, or if this is impossible from adhesions or the situation of the ulcer, the anterior no-loop operation which I first carried out ten years ago and described in 1907,[1] in which a portion of jejunum close to the duodenojejunal flexure is brought through the transverse mesocolon and gastrocolic omentum, and united to the anterior surface of the stomach, the edges of the opening through the great omentum being sutured to the stomach around the anastomosis.

Unless debarred by the situation of the ulcer, the anastomosis should be made to the pyloric segment of the stomach. In the case of ulcers which have produced, or are likely to produce, hour-glass stomach, care should be exercised that the stoma is to their cardiac side. Before performing the anastomosis, the ulcer is carefully examined. Small ulcers I usually invaginate with mattress sutures of silk. If suspicious of malignancy, or if the floor of the ulcer is formed of pancreas or liver, I carry out excision in addition.

[1] Clin. Soc. Tr., 1907, xl, 157.

After excision alone, recurrence of ulceration is common. It should never be done except as a complement to gastrojejunostomy.

When there is indication for excision and the ulcer is large, I believe partial gastrectomy is preferable to simple excision and gastrojejunostomy. During the last two years I have, after closing the duodenum, brought the jejunum at its origin through an opening in the transverse mesocolon and united it directly to the divided cardiac end of the stomach. This makes the operation simpler and shorter; convalescence is as uneventful as when the stomach is closed and a separate anastomosis is carried out.

In no instance have I found it necessary to practice any method of pyloric exclusion.

It has been urged that every chronic gastric ulcer should be excised on account of the possibility of its being or becoming malignant. While I am a firm upholder of the opinion that in a certain percentage of cases carcinoma of the stomach follows directly on chronic gastric ulcer, I believe that promiscuous excision would lead to a greater mortality than that which would follow from the carcinoma that might develop if they were treated by gastrojejunostomy alone.

In none of the cases operated upon for chronic gastric ulcer by gastrojejunostomy alone, in which I had no doubt of the simple nature of the lesion, has carcinoma developed.

On the other hand, in two cases of chronic duodenal ulcer a note was made at the time of the original operation that the ulcer had spread to the stomach; in both, malignant disease of the stomach supervened, and the patients again came under observation on account of fresh gastric symptoms about eighteen months later. I was able to perform partial gastrectomy in one, and the sections showed the growth starting in the edge of a chronic gastric ulcer; in both, the duodenal ulcer had completely healed.

In forty-one cases in which the ulcer was excised as simple, and in all of which serial sections were cut and examined in the London Hospital Pathological Institute, in none was carcinoma discovered. In four of these cases, however, in which excision was carried out on account of the suspicious nature of the

ulcer, carcinoma was starting in the edge of the chronic ulcer in three; the other proved to be a lymphosarcoma.

When hour-glass stomach has supervened, gastrojejunostomy on the central side of the obstruction—single if there is one obstruction only, double if two—is the most satisfactory operation. The indications for excision or partial gastrectomy are the same as in ulcer without this complication.

Acute perforation of a chronic gastric ulcer is a rare event which should be treated, if the condition of the patient admits, by closure or excision of the ulcer followed by gastrojejunostomy.

Hæmorrhage in chronic ulcer calls for operation as soon as possible after the first attack, usually within the first twenty-four hours. The ulcer should be directly treated by ligature of the vessels on each side of it, by inversion or excision followed by gastrojejunostomy.

Treated on these lines the results of the operative treatment of chronic gastric ulcer, both immediate and remote, are excellent. Among 200 cases, excluding those in whom perforation had occurred but including those in whom the immediate indication for operation was hæmatemesis (8 cases, 1 death), there were 6 deaths; the details of operation are given in the appendix.

The results of cases operated upon more than two years by all methods are briefly as follows:

One hundred and twenty-one were operated on more than two years ago with 4 operative deaths; 109 of the survivors were traced for more than two years; 99 of these remained perfectly well, five are better but not quite well. Only one received no relief, one of my early cases, a woman in whom there were extensive adhesions to the spleen and left lobe of the liver, treated by gastrojejunostomy alone. In four patients second operations became necessary, two to excise portions of ulcer which were adherent to the pancreas and two for true jejunal ulceration.

There is no difference whatever in the results in those cases operated on for ulcer at a distance from the pylorus and those at the pylorus, or in those in which the ulcer was excised in addition to gastrojejunostomy.

I know of no case in which fresh ulceration occurred except after excision alone or in which recurrence of symptoms took place after a lapse of more than two years.

In conclusion I would say that gastrojejunostomy still remains the operation of choice in chronic duodenal ulcer and in the large proportion of cases of chronic gastric ulcer; it is only when complications have arisen that excision has to be added to the operative treatment.

Appendix A

Up to July 20, 1914, I had operated upon two hundred cases of unperforated chronic gastric ulcer, with six deaths.

The following were the operations performed (twenty-three complicated by hour-glass stomach are separately tabulated):

Excision alone. Six cases. One death (a patient in whom transgastric excision was carried out. He developed a subphrenic abscess and died several weeks later).

Excision and gastrojejunostomy. Twenty-four cases. No deaths.

Partial gastrectomy. Nine cases. Two deaths; one from acute gastric dilatation, one from subphrenic abscess.

Gastrojejunostomy alone, or combined with "inversion." One hundred thirty-eight cases. Two deaths (one from hæmatemesis, the result of erosion of the splenic artery two days after operation, the other from pneumonia nine days after operation).

In the twenty-three cases of hour-glass stomach the following were the operations carried out:

Single gastrojejunostomy. Eighteen cases. One death, twelve days after operation—a patient who had been having repeated severe attacks of hæmatemesis. At post-mortem it was found that there was no attempt at union of the anastomosis.

Double gastrojejunostomy. Two cases. No death.

Partial gastrectomy. Three cases. No death.

Taking all cases operated upon more than two years by all methods, the results are as follows: One hundred twenty-one have been operated on more than two years with four operative deaths. I have been able to investigate the present condition of ninety-five; of these, eighty-five are in perfect health and have had no recurrence of symptoms, five are better, one no better.

Second operations were carried out for recurrence of symptoms in four patients; in two, to excise posterior unhealed portions of saddle-shaped ulcers twelve months and sixteen months after gastrojejunostomy.

In two males it became necessary for jejunal ulcer three months and two years after operation. The latter had severe pain and I operated on him with great reluctance, as he was also suffering from advanced genito-urinary tuberculosis. He died sud-

denly four days after operation and no abdominal cause was discovered at the post-mortem examination. The operation in the former was carried out over two years ago; he remains quite well. In both patients the ulcer had been excised in addition to gastrojejunostomy.

Five died from other diseases, remaining quite well more than two years; two died at eight, one at seven, and two at three years after operation; one died at eighteen, and two at ten months after operation, from other causes. I have failed to trace the remainder, but nine of them I watched for more than two years; one, five years after operation, was better, but not quite well; the others were quite well at seven, six, five, four, three, and two years.

Appendix B

In 1912 [1] I published the late results in twenty-one cases of non-obstructive ulcer treated by gastrojejunostomy alone. Fifteen were quite well at periods varying from two to eight years; two had died from other causes two and three years after operation having had entire relief; three were almost well; and only one, a woman who had had a large ulcer at the cardiac end of the stomach, adherent to the spleen, had obtained no relief.

Seventy-eight cases of this type, treated by gastrojejunostomy without excision, have now been operated on more than two years. There was one death from bronchopneumonia nine days after operation. I have been able to ascertain the present condition of sixty-six: fifty-four are and have remained perfectly well at the following periods: nine years, three; eight years, one; seven years, three; six years, four; five years, seven; four years, ten; three years, thirteen; two years and over, thirteen; and they have needed no further treatment. Seven died of causes other than gastric, remaining perfectly well till death; one seven years, one, four years, two, three, years, one, two years, one, eighteen, and one six months, after operation. Three were lost sight of when quite well four years after operation, one after two years, one after one, and two after a few weeks.

Two patients had to be operated on again and ulcers excised which had perforated and were adherent to pancreas. In both, the original ulcer had been saddle-shaped; the anterior portion and that on the lesser curvature had completely healed. In one, ten months after gastrojejunostomy for a large saddle-shaped ulcer on the lesser curvature, I removed gall-stones; the ulcer had healed. That is now four years ago and the patient remains in perfect health. In two other cases I had to operate about two years later and removed chronically inflamed appendices; these ulcers had also completely healed. If these are included, the number of those quite well is 57. Six of the others are much better, and only one, previously mentioned, is unrelieved. In no instance did malignant changes supervene.

Of 77 who survived the operation, 66 are or remained quite well for more than two years after operation, six are much better but not quite well, two required further operative treatment, one was not relieved; the remainder were lost sight of within the first two years after operation or died during this period of causes unconnected with the stomach

[1] Lancet, Lond., 1912, July 13.

ANKYLOSIS: AN EXPERIMENTAL STUDY[1]

By NATHANIEL ALLISON, M. D., F. A. C. S., Saint Louis
Associate in Orthopedic Surgery, Washington University
AND
BARNEY BROOKS, M. D., Saint Louis
Assistant in Surgery, Washington University
From the Surgical Laboratory of Washington University Medical School, Saint Louis

THIS experimental study was undertaken for the purpose of investigating the changes that take place in the tissues of the joint during the process of ankylosis. In a previous study (1) on the mobilization of ankylosed joints, it was observed that there was a marked difference in the reaction to injury between epiphyseal and diaphyseal bone. In the experiments reported there was fibrous union between two denuded joint surfaces at the end of sixty days. At the end of this time there was no evidence of bony ankylosis. A further study of this process was carried out in the experiments here reported with the belief that the facts gained will aid in the surgical treatment of ankylosed joints.

Hoffa (2) has defined ankylosis as the condition in which two or more joint surfaces become bound together and immovable. He distinguished three types: an intercartilaginous fibrous ankylosis, an interosseous fibrous ankylosis, and an osseous ankylosis. True bony ankylosis, according to Hoffa, may be produced in two ways: sometimes there is transformation of the connective tissue of a fibrous ankylosis directly from a cartilage metaplasia; at other times, following the destruction of cartilages from inflammatory diseases, bony union develops from the bone-marrow and periosteum.

Nichols and Richardson (3), from the study of sixty-seven cases of non-tuberculous arthritis, divide this condition into two types; namely, a proliferative type and a degenerative type. In the degenerative type there is a tendency to destruction of joint-cartilage with deformity and no ankylosis. An arthropathy, such as a Charcot joint, is typical of this class. In the proliferative type there is destruction of joint-cartilage leading to ankylosis of adjacent joint structures; the earliest change is a proliferation of the synovial membrane at the insertion of the joint-capsule. This leads to a pannus growth which advances over the cartilage, at times, uniting the two joint surfaces and destroying the underlying cartilage. Accompanying this process there may be destruction of the joint-cartilage on its epiphyseal surface by granulation tissue from the marrow spaces. These investigators believe that the destruction of cartilage by the pannus growth predominates, though either process leads to fibrous ankylosis. True bony ankylosis, according to Nichols and Richardson, may be produced in three ways: in certain instances there is a proliferation of the perichondrium, which is readily transformed into cartilage or bone; in other instances new bone production results from osteoblasts which have their origin in the bone-marrow; finally, in rare instances there is a direct transformation of fibrous tissue into bone.

Axhausen and Pels (4) and Kroh (5) have described joint changes resulting from injury in experimental studies of arthritis deformans. In the literature above referred to, various joint changes have been described, but the sequence of these changes and the duration of the ankylosing process have not been made clear.

The object of these experiments was the study of the nature, sequence, and duration of the tissue changes which lead to bony ankylosis. In these experiments the knee-joints of dogs were used. All experiments were done under complete ether anæsthesia. All operations were done under a careful aseptic technique. Post-operative care of the animals used was such as to insure as little suffering as possible. All animals were sacrificed with chloroform. Four experimental methods were used.

[1]Read before the Orthopedic Section, American Medical Association Atlantic City, June 23, 1914.

I. Partial excision of joints, eight experiments.

II. Destruction of joint-cartilage, three experiments.

III. Injury to joint-cartilage, two experiments.

IV. Direct infection of normal joints, seven experiments.

I. PARTIAL EXCISION OF JOINT

The knee-joint was opened by a lateral longitudinal incision, the patella and its tendon were displaced medialward, the cruciform ligaments were divided. The knee was completely flexed and 1 cm. of the lower end of the femur and 0.5 cm. of the upper end of the tibia removed with a saw. The joint was then closed with interrupted fine silk sutures and held fixed by a plaster of Paris dressing.

Experiment No. 10. Partial excision of knee-joint. Third day: Dog well; plaster in good condition. Sixth day: Dog well; sacrificed. Knee-joint removed and capsule opened by a circular incision. The bones are in good apposition. Between the bone-ends there is a layer of fresh granulation tissue about 1 mm. in thickness, which can be easily separated from the bones. Joint fixed in formalin. Microscopical sections prepared.

Microscopical study. Sections show the bone-ends to be separated by a thin plate of fibrin. There is a narrow zone of granulation tissue along the free margins of the bone surfaces. There are new blood-vessels growing out into the fibrin accompanied by strands of fibroblasts. There are numerous small fragments of bones which are necrotic and which are surrounded by large polynuclear phagocytic cells. In a few places there are small islands of osteoid tissue which seem to represent bone destruction. There is no new bone formation. The bone-marrow of the epiphyses is very rich in lymphoid cells, except for a narrow zone along the cut margin of the bone which contains few lymphoid cells.

Experiment No. 1. Partial excision of knee-joint; bones sutured in apposition by two silver wires. Fifth day: Animal in good condition. Ninth day: Animal found dead; autopsy failed to reveal cause of death. Operative wound healing *per primam*. Joint removed, fixed in formalin, and decalcified.

Microscopical study. A median longitudinal section through the joint shows the bones in good approximation (Fig. 1). The epiphyses are incompletely ossified. The space between the ends of the bones is filled in large part by blood-clot, which is being organized by granulation tissue growing from the marrow spaces (Fig. 2). Scattered through the blood-clot are numerous bone fragments which show evidence of absorption. No new bone formation; no regeneration of cartilage. At the margin of the condyle there are small processes of granulation tissue growing from the marrow into the cartilage. The saw-cut in the tibia has gone through the posterior aspect of the epiphyseal line, and here there is a small nodule of new-formed bone.

Experiment No. 3. Partial excision of knee-joint. Fourteenth day: Dog well; plaster bandage in good condition. Nineteenth day: Animal found dead; cause not known. Operative wound healed *per primam*. Joint removed and microscopical preparation made.

Microscopical study. Ends of bones in good position. The space between varies from 1 mm. to 5 mm. The tissue between the bone-ends is composed of moderately densely packed spindle-cells, among which there are numerous large, thin-walled blood-vessels. Midway between the bones there is a small area of a densely eosin-staining fibrin network, evidently old unorganized blood-clots. Scattered here and there are small fragments of bone which are being absorbed. The ends of the bones show the cancellous bone exactly as left by the saw. There is no new bone formation. There is complete fibrous ankylosis (Fig. 3).

Experiment No. 4. Partial excision of knee-joint; bones held in apposition by a silk ligature and plaster of Paris dressing. Seventh day: Dog in good condition; plaster bandage intact. Twenty-first day: Dog in good condition; plaster bandage removed. Passive motion present; operative wound healed *per primam*. Thirty-fifth day: Dog in good condition; knee held flexed; extension limited. Fiftieth day: Animal sacrificed; knee-joint removed. Specimen allows free motion in

flexion; extension is checked at 20 degrees from complete. No lateral motion.

Microscopical study. Section shows that the cut ends of the bones are not in close apposition. The tibia is flexed, and the patellar tendon lies over the cut surface of the femur, to which it is adherent by a mass of fibrous tissue (Fig. 4). The joint cavity is entirely obliterated by a mass of dense fibrous tissue. In this mass are two irregular slitlike cavities, lined with cells that have the characteristics of synovial endothelium (Fig. 5). It seems probable that it is such spaces as these that have been interpreted as artificial joint cavities resulting from the interposition of various substances (Sumita [6]). There is no new bone formation, and no regeneration of cartilage.

Experiment No. 8. Partial excision of knee-joint. Seventh day: Animal well; plaster bandage in good condition. Fifteenth day: Plaster bandage removed; operative wound healed *per primam;* joint allows free motion. Plaster bandage reapplied. Twenty-third day: Plaster bandage in good condition; radiogram taken through plaster bandage shows bones held in apposition at 60 degrees flexion. No evidence of bony union. Thirty-fifth day: Plaster bandage removed; knee not swollen or tender; passive motion allowed through 45 degrees. Plaster bandage reapplied. Forty-fourth day: Plaster bandage removed; small amount of motion; animal in good condition. Plaster bandage reapplied. Sixty-fourth day: Plaster bandage in good condition; animal well. Sacrificed; plaster bandage removed from limb. Radiogram (Fig. 6) taken shows no evidence of bony union. Microscopical preparation made.

Microscopical study. Sections show bones in close apposition (Fig. 7). The joint cavity between femur and tibia is entirely obliterated. The space between the femoral condyles and the patella remains. The femur and tibia are joined by a mass of dense fibrous tissue containing relatively few blood-vessels. There is no bony union. Along the margins of the cut surfaces of femur and tibia the trabeculæ are markedly thickened. The marrow spaces here contain numerous thin-walled blood-vessels and few lymphoid cells. At the junction of the cancellous bone and fibrous tissue there are numerous multinucleate granular cells. The cartilage over the anterior surface of the condyles and patella is thin. Between the femur and patella there are numerous villi composed of myxomatous tissue and covered with synovial endothelium.

Experiment No. 2. Partial excision of knee-joint. Silver wire suture used to hold bones in apposition; plaster of Paris bandage. Fifth day: Animal well; foot swollen. Plaster bandage removed; limb put in splint bandage. Sixteenth day: Wounds healed; dog well. Limb held flexed; knee-joint thickened; very little motion, with crepitus. Sixty-fourth day: Dog well; knee stiff. Radiogram (Fig. 8) taken shows a suggestion of bony union. Eighty-sixth day: Dog sacrificed; knee-joint removed. Microscopical sections prepared.

Microscopical study. Sections show the bones in good apposition (Fig. 9). The femoral epiphyseal line is intact, but the saw-cut in the tibia has passed through the epiphyseal line. There is no bony union. The bones are united by a mass of dense fibrous tissue within which there are several small slitlike cavities lined with flattened cells, similar to those described in Experiment No. 4.

Experiment No. 7. Partial excision of knee-joint. Silver wire suture used to hold bones in apposition; plaster of Paris dressing. Fourth day: Joint slightly swollen and tender; plaster removed; small amount of discharge. Thirteenth day: Dog in good condition; slight discharge from wound. Twenty-first day: Dog in good condition; wound healed. Thirtieth day: Dog well. Radiogram taken; bones in poor position; head of tibia dislocated medialward; flexion of 60 degrees. Fiftieth day: Dog well; knee allows very little motion. One hundred and twentieth day: Dog well; knee stiff. One hundred and forty-sixth day: Dog sacrificed; knee-joint removed. Joint is thickened; specimen allows slight motion at joint. Microscopical sections prepared.

Microscopical study. Median longitudinal section cut. The joint cavity is entirely obliterated. The patella is of normal shape. It is united to the femur by a mass of dense fibrous tissue. The joint-cartilage of the patella has disappeared except for a few small

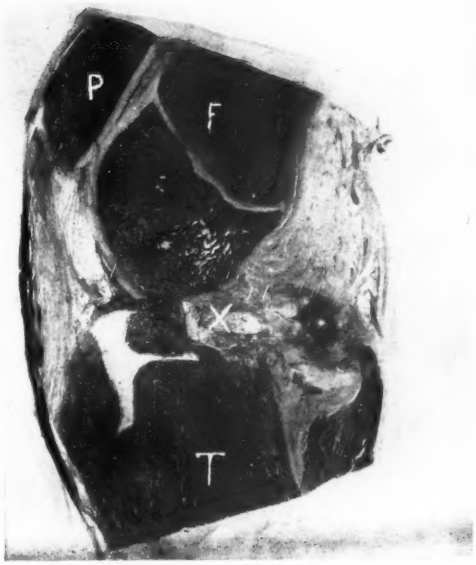


Fig. 1. Experiment No. 1. Partial excision of knee-joint; 9 days. Median longitudinal section of entire joint. F, femur; T, tibia. The space between the ends of the bones, X, is filled with organizing blood-clot.

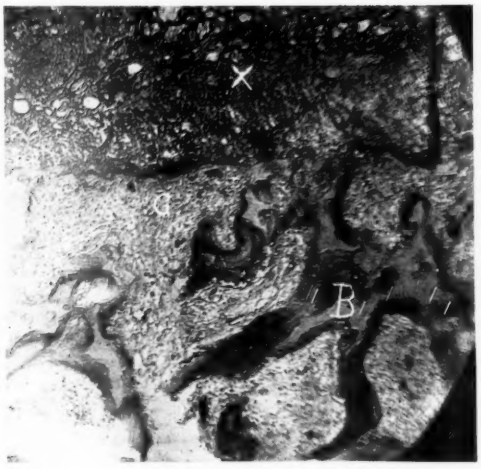


Fig. 2. Experiment No. 1. High-power photomicrograph of the edge of the femur adjacent to X shown in Fig. 1. B, cancellous bone of the epiphyses of the femur; X, old blood-clot; G, granulation tissue in the marrow.

areas, which show a marked change. The lower end of the femoral diaphysis has undergone marked atrophy, being separated completely from the epiphysis. The femoral epiphysis is joined to the tibia by a mass of dense fibrous tissue which contains very few blood-vessels. At the junction of this fibrous tissue and the cancellous bone of both the femur and tibia there is a zone of tissue which contains numerous large blood spaces. The cells which make up this tissue are spindle-cells arranged in strands and whorls about the blood spaces. Scattered here and there are bone fragments which are being absorbed. In other areas the connective-tissue cells are encapsulated, and there is a hyaline intercellular matrix in which there is a deposit of calcium salts. These areas are the same as in Fig. 18.

Experiment No. 5. Partial excision of knee-joint; joint fixed in complete extension in plaster of Paris bandage. Twenty-seventh day: Operative wound healed; knee allows slight motion; plaster of Paris dressing removed. Fortieth day: Dog in good condition; joint stiff. Radiogram shows excellent position; bones in apposition in complete extension (Fig. 11). One hundred and eighteenth day: Dog has been in good condition; knee is stiff. Animal sacrificed; knee-joint removed. Radiogram (Fig. 12) shows bony union. Microscopical sections prepared.

Microscopical study. Median longitudinal sections show joint cavity obliterated except for a very small slitlike space between the quadriceps tendon and the anterior surface of the femur. The joint-cartilage of the patella has been completely replaced by fibrous tissue. The femur and the tibia are joined by cancellous bone. The line of union is only distinguished by slightly thickened and irregular trabeculæ (Fig. 13).

Summary. In these experiments in which the joint was partially excised and the cancellous bone surfaces of the epiphyses were approximated, there was produced the simplest experimental condition for the study of the development of bony ankylosis. This condition is the same as that which is produced in a surgical operation for the mobilization of an osseous ankylosis.

These experiments show that ankylosis by bone is a process which develops slowly.

Fig. 3.

Fig. 4.

Fig. 3. Experiment No. 3. Partial excision of knee-joint; 19 days. Median longitudinal section of entire joint. P, patella; F, femur; T, tibia. The tissue X, between the ends of the bones, is new-formed connective tissue. No new bone formation.

Fig. 4. Experiment No. 4. Partial excision of the knee-joint; 50 days. Longitudinal section through the internal condyle of the femur. F, femur; T, tibia; Pt, patellar tendon. The ends of the femur and tibia are not in apposition. The lower end of the femur is adherent to the patellar tendon. Note that the lower end of the femur is a straight line, which shows no new bone formation. Note also the irregular spaces between the femur and the tibia. See Fig. 5.

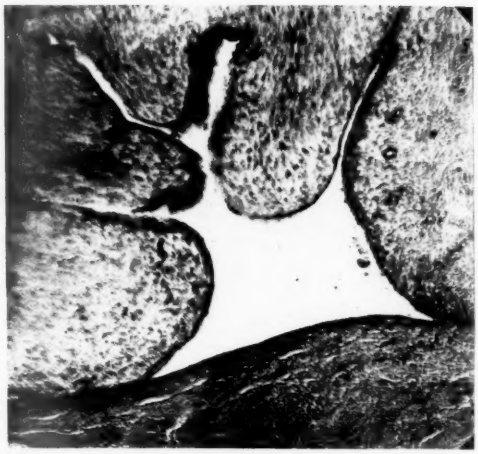


Fig. 5. Experiment No. 4. Partial excision of knee-joint; 50 days. High-power photomicrograph of the small space in the fibrous tissue between the femur and tibia indicated, S, in Fig. 4.

At the end of six days (Experiment No. 10) the apposed bones were united by a fibrous exudate into which is growing granulation tissue from the bone-marrow. At the end of nineteen days (Experiment No. 3) the bones are united by connective tissue. In Experiments Nos. 4, 8, and 2, of fifty, sixty-four, and eighty-six days respectively, the connective tissue uniting the bones became progressively more fibrous in character. At the end of one hundred and forty-six days (Experiment No. 7) the fibrous ankylosis was being changed into an osseous ankylosis by a direct transformation of the fibrous tissue into bone. In Experiment No. 5, after one hundred and eighty days with close approximation of the bone surfaces, the ankylosis was by bone.

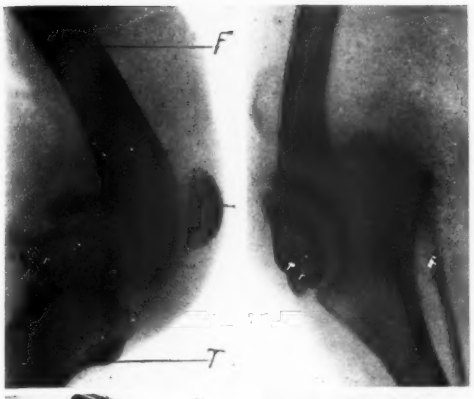
II. DESTRUCTION OF JOINT-CARTILAGE

The knee-joint was opened by a lateral longitudinal incision; the patella and its tendon were displaced medialward. The semilunar cartilages were removed from the head of the tibia, and the joint-cartilage was curetted from the joint surfaces of the tibia, femoral condyles, and patella. The joint was closed with interrupted fine silk sutures. The limb was held fixed in a plaster of Paris dressing.

Experiment No. 15. Destruction of joint-cartilage. Fifth day: Animal in good condition. Eleventh day: Animal has cough and nasal discharge. Sacrificed; plaster dressing removed; healing *per primam*. Joint removed; fixed in formation. After decalcification the joint was sectioned longitudinally. The joint cavity was entirely obliterated by granulation tissue, except for a small slitlike space between the patella and the anterior femoral surface. There is no gross evidence of new bone formation.

Microscopical study. Between the denuded bones there is a mass of fibrin, which contains numerous small fragments of bone. From the marrow there is an active proliferation of new blood-vessels and fibroblasts. No new-formed bone (Fig. 14).

Experiment No. 14. Destruction of joint-cartilage. Fifth day: Animal in good condition. Eleventh day: Plaster dressing in good shape; animal has l st weight. Twenty-first day: Animal found dead; cause not discovered. Joint removed. After decalcification the joint was sectioned longitudinally. There



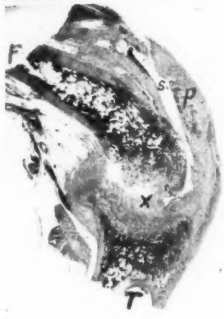


Fig. 6. Fig. 8.
Fig. 7. Fig. 9.

Fig. 6. Experiment No. 8. Partial excision of knee-joint; 64 days. X-ray photograph. F, femur; T, tibia; P, patella. Note that the ends of the bones are not distinctly separate. Compare with Fig. 8.

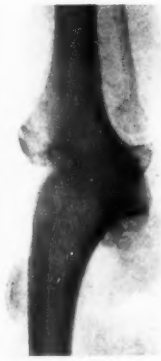
Fig. 7. Experiment No. 8. Partial excision of knee-joint; 64 days. Median longitudinal section of entire joint. F, femur; T, tibia; P, patella; S, joint cavity between femur and patella which is preserved. The tibia and femur are united by a mass of dense fibrous tissue (X).

Fig. 8. Experiment No. 2. Partial excision of knee-joint; radiogram 64 days after operation. There is apparently bony ankylosis.

Fig. 9. Experiment No. 2. Partial excision of knee-joint; 86 days. Longitudinal section of entire joint. F, femur; T, tibia. The bones are joined by a mass of dense fibrous tissue.

was complete obliteration of the joint cavity, except at posterior margin, where a small piece of cartilage remained.

Microscopical study. The cartilage has been completely removed from the femur and patella; some cartilage remains at posterior margin of the tibial joint surface (Fig. 15). The denuded bones are joined by a mass of newly formed fibrous tissue, which is growing



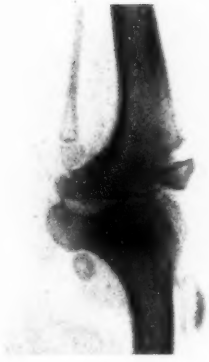


Fig. 11. Fig. 12.

Fig. 11. Experiment No. 5. Partial excision of knee-joint; radiogram 40 days after operation. Note the close approximation of the ends of the femur and the tibia, and the absence of union by bone.

Fig. 12. Experiment No. 5. Partial excision of the knee-joint; radiogram 180 days after operation. There is an osseous ankylosis.

from the marrow spaces of the cancellous bone. There are a few areas of old blood-clots which are being invaded by proliferative blood-vessels and fibroblasts (Fig. 16). There is no new bone formed from the epiphysis. In striking contrast there is a well-marked area of subperiosteal new bone formation on the anterior surface of the femoral diaphysis (Fig. 12).

Experiment No. 22. Destruction of joint-cartilage, limited to anterior surface of femur and under surface of the patella. Third day: Entire leg swollen; plaster dressing changed. Seventh day: Leg still swollen; plaster dressing removed. Twelfth day: Purulent discharge from wound; animal in good condition. Eighteenth day: Wound closed; discharge has ceased. Thirty-fifth day: Wound entirely healed; limb held flexed; passive motion free. Forty-eighth day: Animal in good condition; passive motion limited. Three hundred and thirty-fourth day: Animal in good condition; sacrificed. There is slight motion between femur and tibia; the patella is fixed. Joint removed; microscopical sections prepared.

Microscopical study. Median section through the joint shows entire obliteration of the space between the patella and its tendon and the anterior surface of the femoral

Fig. 13. Experiment No. 5. Partial excision of the knee-joint, 180 days after operation. Median longitudinal section of the joint. F, femur; T, tibia; P, patella. The cancellous bone of the tibia and femur is continuous.

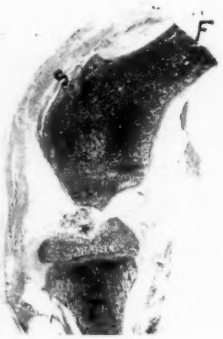


Fig. 14.

Fig. 15.

Fig. 14. Experiment No. 15. Destruction of joint cartilage; 11 days. Longitudinal section of entire joint. F, femur; T, tibia. The joint-cartilage has been completely removed from the femur. The joint cavity between the femur and the joint-capsule has been completely obliterated by granulation tissue. The space S is a tear in the section.

Fig. 15. Experiment No. 14. Destruction of joint-cartilage; 21 days. Median longitudinal section of entire joint. F, femur; T, tibia; P, patella. The joint-cartilage has been entirely removed from the femur and patella. Note the complete obliteration of the joint cavity. See Fig. 16.

condyles. There are a few small slitlike cavities between the femur and the tibia. There is a small portion of the femoral joint-cartilage remaining on the posterior margin of the femoral condyles. On the tibia the cartilage has undergone a fibrous transformation. Between the patella and the femur there is a mass of dense fibrous tissue which contains numerous large blood-spaces (Fig. 17). At the junction of the bone and this fibrous tissue there are areas that show a gradual transition between bone and fibrous tissue, so that it cannot be said where bone and fibrous tissue begin and end. The fibrous tissue near the margins of the actual bone shows a remarkable architectural appearance in that the arrangement of the connective-tissue fibers and cells is in the form of whorls around blood-spaces, similar to the structure of cortical bone. There is no new bone formation in the sense of cartilage destruction and replacement by bone formed by osteoblasts; but there is a metaplasia of the fibrous tissue into fibrocartilaginous tissue followed by a direct transformation into bone. The new bone formed in this process has the architecture of cortical rather than of cancellous bone (Fig. 18).

Summary. In these experiments in which the articular cartilage was destroyed the condition produced was essentially the same as that in which partial excision was done, except that the normal contour of the bones was unchanged. This condition is the same as that which follows a surgical operation for the mobilization of an ankylosis in which the bones have retained their normal shape — such as is found in fibrous ankylosis.

These experiments show that after destruction of joint-cartilage there is union of the joint surfaces by connective tissue which is transformed into bone only after a relatively long time.

In Experiment No. 22, actual union by bone was not complete at the end of 334 days.

III. INJURY TO JOINT-CARTILAGE

Experiment No. 23. Knee-joint opened in the usual manner. With a curette small

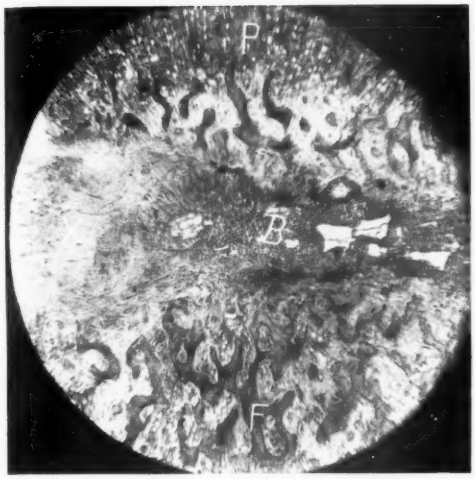


Fig. 16. Experiment No. 14. Destruction of joint-cartilage; 21 days. Photomicrograph of junction of the patella and femur. P, cancellous bone of patella; F, cancellous bone femur. The two bones are adherent by fibrinous exudate at B, which has been replaced by fibrous tissue at X. Note the complete absence of new bone formation.

Fig. 17. Experiment No. 22. Destruction of joint-cartilage; 334 days. Median longitudinal section through entire joint. F, femur; T, tibia; P, patella. The patella is adherent to the femur by a mass of dense fibrous tissue (X) which is becoming ossified. See Fig. 15.

areas of cartilage were removed from the inferior surfaces of the femoral condyles and from the outer surface of the tibial head. The joint was closed as usual. No plaster of Paris dressing was applied. Eighth day: Operative wound healed *per primam;* knee slightly swollen, not tender. Animal in good condition; passive motion of 45 degrees allowed. Fortieth day: Animal found dead; autopsy shows bronchopneumonia. Knee removed; microscopical preparations made.

Microscopical study. Longitudinal section through the outer femoral condyle and tibia shows that the cartilage was destroyed in areas of 1 cm. diameter on the femoral and tibial surfaces. The two denuded areas are not in apposition. Overlying these denuded areas is an old fibrous exudate which is being replaced by granulation tissue from the marrow. In the marrow in the regions of these injuries there is an active production of granulation tissue which is absorbing the cartilage from below. The synovial membrane shows a marked thickening due to proliferation of the endothelial cells, and infiltration by small round-cells.

Experiment No. 27. Knee-joint opened in the usual manner and patella fractured transversely. Wound closed; no plaster of Paris bandage applied. Wound healed *per primam.* Animal used limb with no disability. Three hundred and sixty-fifth day: Animal sacrificed. Passive motion gives slight crepitus. Joint opened; no excess of free fluid; fracture has healed to linear scar. Extending across the joint cavity in various directions are translucent fibrous bands. The cartilage on the tibia, on the inferior surface of the condyles, and in the intercondylar groove seems normal. On the lateral medial and superior margins of the cartilage on the femur there is a marked change in the cartilage: it appears much thinned or replaced by fibrous tissue.

Microscopical study. Medial longitudinal section shows normal cartilage, except at the upper margin of the femoral surface. Here the cartilage is entirely destroyed, the cancellous bone being covered by a layer of fibrous tissue. The synovial membrane is thickened and shows an infiltration of small round-cells. There are numerous villi which are seen especially around the margins of the cartilage.

Summary. In these experiments the injury to the joint-cartilage was comparatively slight.

Fig. 18. Experiment No. 22. Destruction of joint-cartilage; 334 days. Photomicrograph of the junction of the bone and fibrous tissue indicated (X) in Fig. 17. The picture shows well-developed bone at B and dense fibrous tissue at A. Between these there is a cone (C) in which the fibrous tissue is being converted directly into bone.

In Experiment No. 23, fourteen days after the destruction of a small area of joint-cartilage, there was an inflammatory process in the joint which was destroying the cartilage in a manner exactly similar to that which follows infection of the joint cavity. In Experiment No. 27, in which the joint injury was limited to a transverse patellar fracture, there were after three hundred and sixty-five days definite pathological changes in the joint-cartilage and synovial membrane.

IV. DIRECT INFECTION OF NORMAL JOINTS

In these experiments the organisms were injected directly into the knee-joint cavity with an hypodermic syringe. The organisms used were a staphylococcus aureas, obtained from a fatal case of pyæmia in man, and a bacillus tuberculosis of the human type, which had been grown in the laboratory for several years. Of the staphylococcus aureas, twenty-four hour broth cultures were used for injection. Of the tubercle bacilli, one month glycerine agar cultures were suspended in normal salt solution.

Experiment No. 19. Injection of 2.5 ccm. broth-culture staphylococcus aureas into knee-joint cavity. Second day: Animal in good condition; knee swollen, tender, and hot. Third day: Animal sick; knee swollen and tender. Fourth day: Animal dead; autopsy shows extensive consolidation of the lung with miliary abscesses. Joint removed; when opened the capsule was adherent in several places to the lateral and medial sides of the condyles. There is no beginning cartilage destruction about the margins of the cartilage. Microscopical preparations made.

Microscopical study. A transverse section of the condyles (Fig. 19) shows the capsule adherent to the lateral surface of the condyle by inflammatory exudate, obliterating the greater part of the lateral joint cavity. A median longitudinal section shows the cartilage intact, except at the margins of the patella and at the posterior margin of the cartilage on the femur. Here there are small areas in infiltration with leucocytes, some necrosis, and a fibrinous exudate (Fig. 21). The cancellous bone of the condyles and patella appears normal. Extending from the marrow into the under surface of the joint-cartilage are numerous buds of inflammatory tissue (Fig. 22) containing a large number of leucocytes. The free surface of the cartilage is strikingly regular in outline. In some areas the cartilage nuclei nearest the joint surface have lost their staining properties, and the matrix is more opaque and takes a deeper eosin stain. Over such areas there is a thin layer of adherent fibrinous exudate. There is a very active proliferation of the synovial endothelium (Fig. 20).

Experiment No. 17. Injection 2.5 ccm. broth culture of staphylococcus aureas into knee-joint. Second day: Animal in good condition; knee swollen, tender, and hot. Third day: Local heat and swelling; motions of knee guarded. Thirteenth day: Animal found dead; cause not discovered. Knee-joint removed and opened by lateral incision. There are areas of infection and ulceration about the edges of the cartilage; cartilage elsewhere is normal in appearance. Joint contains no excess of free fluid. Microscopical study not made.

Experiment No. 13. Injection 2 ccm. broth culture of staphylococcus aureas into knee-

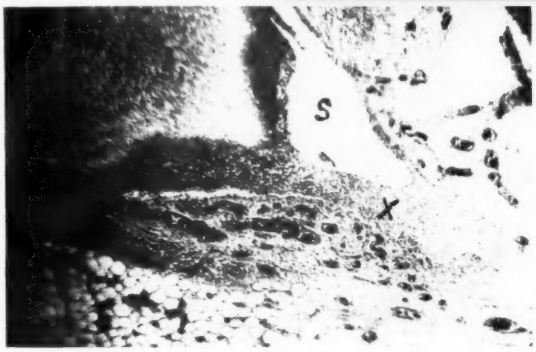


Fig. 19.

Fig. 20.

Fig. 21.

Fig. 22.

Fig. 19. Experiment No. 19. Infection of joint cavity; 4 days. Cross-section of one condyle and half of patella. F, femur; P, patella; E, fibropurulent exudate. The site of the joint between the condyle and capsule. With the organization of such an exudate the joint cavity is diminished by the attachment of the joint capsule at the point B rather than its normal attachment at A.

Fig. 20. Experiment No. 19. Infection of joint cavity; 4 days. Photomicrograph to show the marked proliferative process in the synovia. S, joint cavity; X, synovia.

Fig. 21. Experiment No. 19. Infection of joint cavity; 4 days. Photomicrograph of the posterior margin of the joint-cartilage in the intracondylar groove. S, joint cavity; C, cartilage. At the junction of the synovia and the cartilage note marked proliferation of the synovial endothelium and the beginning destruction of the cartilage at D.

Fig. 22. Experiment No. 19. Infection joint cavity; 4 days. Photomicrograph of the line of union of the joint-cartilage and the cancellous bone of the epiphysis. C, cartilage; B, cancellous tissue; X indicates small budlike growths of granulating tissue invading the cartilage.

joint. Fifth day: Animal in good condition; knee swollen and tender; motion limited. Fourteenth day: Animal in fair condition; knee-joint hot and tender; fluid in joint; motion limited. Seventeenth day: Dog has lost weight; knee thickened, not so tender; uses limb slightly in walking. Twenty-first day: Animal has sore eyes; sacrificed. The knee is thickened. Joint opened. There is a slight excess of joint fluid which is cloudy and gelatinous. Culture taken from this fluid grew staphylococcus aureas. At the margin of the cartilage on the internal condyle there is an irregular erosion about 0.5 cm. in diameter, the margins of which were intensely injected. Around the margin of the patella there was erosion of the cartilage. The patella tendon was joined to the anterior surface of the femur by a band of friable, translucent, œdematous granulation tissue. The capsule

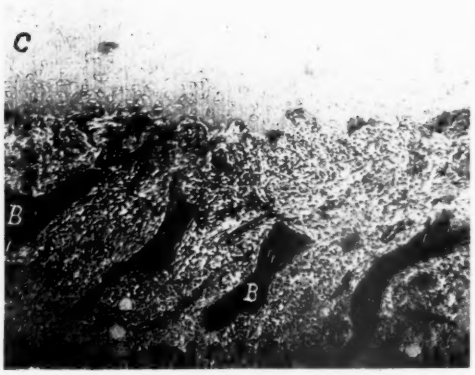


Fig. 23. Experiment No. 13. Infection of joint cavity; 21 days. Photomicrograph showing destruction of cartilage by granulation tissue from its under surface. This is at a distance from the actual ulceration of the cartilage. Note that the cartilage (C) is separated from the cancellous bone (B) by a zone of granulation tissue. At this stage the cartilage can be readily lifted off the bone.

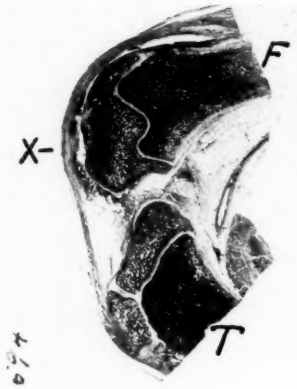


Fig. 24. Experiment No. 13. Infection of joint; 21 days. Longitudinal section through internal condyle. F, femur; T, tibia. Note the ulceration of the cartilage at X. See Figs. 25, 26, 23.

is everywhere œdematous. Microscopical sections prepared.

Microscopical study. There is a fibropurulent exudate in the joint cavity. The quadriceps tendon is adherent to the anterior surface of the femur. The surface of the joint-cartilage of the femur is normal except for the margin, where there is everywhere a beginning cartilage destruction and at a point on the medial condyle there is complete destruction over an area of 0.5 cm. in diameter (Fig. 24). The cartilage on the patella and tibia shows a similar condition. The under surface of the cartilage shows a strikingly abnormal picture. There is a narrow zone in the cancellous bone immediately under the cartilage in which there is a marked decrease in the lymphoid cells with numerous proliferating blood-vessels, fibroblasts, and leucocytes. From this zone of granulation tissue there extends into the cartilage numerous budlike processes. The bone trabeculæ show evidence of destruction (Fig. 23). The synovial membrane shows marked proliferation of large, pale, endothelial-like cells which form villi extending into the joint cavity.

Experiment No. 12. Injection 1 ccm. broth culture of staphylococcus aureas into knee-joint. Fifth day: Knee slightly swollen and tender; animal in good condition. Fourteenth day: Animal used limb with slight limp; no swelling or heat. Seventeenth day: Animal uses limb normally. Injection 4 ccm. broth culture of staphylococcus aureas. Twenty-first day: Limb held flexed; slightly swollen and tender. Twenty-eighth day: Animal in good condition; joint slightly hot and tender, extension limited. Injection 2.5 ccm. staphylococcus aureas broth culture. Twenty-ninth day: Knee swollen, fluctuates; animal in good condition. Forty-first day: Dog in good condition; no local heat or swelling. Injection of 2 ccm. of broth culture of staphylococcus aureas. Forty-fourth day: Animal in good condition; joint swollen, tender, not used. Fifty-sixth day: Animal holds knee flexed; no heat or swelling. Injection of 2.5 ccm. broth culture staphylococcus aureas. Sixty-second day: Animal in good condition; no swelling or tenderness. Animal sacrificed. On opening the knee-joint there was 3 to 4 ccm. of a thick cloudy fluid. About the margin of the patella is a narrow zone of villous granulation. At the superior margin of the femoral cartilage there is an area of destruction. About the insertion of the capsule there are numerous polyplike granulations. The central portions of the joint-cartilage are not normal.

Experiment No. 11. Injection 1 ccm. broth-culture staphylococcus aureas into knee-

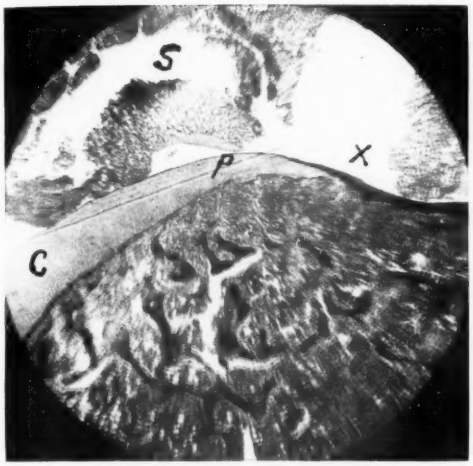


Fig. 25. Experiment No. 13. Infection of joint; 21 days. Photomicrograph of margin of ulceration of cartilage. S, joint cavity. The cartilage is completely destroyed at X. Note the notching of the cartilage from its under surface at P. Also that the joint surface of the cartilage remains quite smooth.

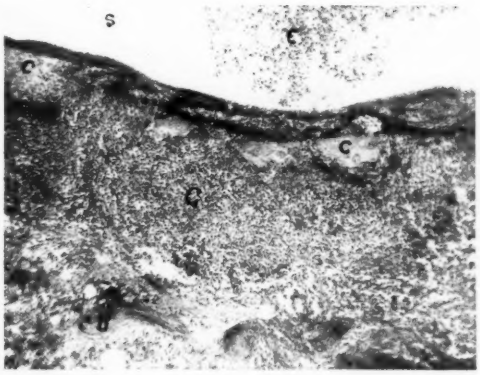


Fig. 26. Experiment No. 13. Infection joint cavity; 21 days. Photomicrograph to show almost complete cartilage destruction. S, joint cavity; C, small remnants of joint-cartilage; B, spicule of cancellous bone; G, granulation tissue.

joint cavity. Fifth day: Knee slightly swollen; animal uses leg in walking. On the 17th, 28th, 41st, 56th, and 64th days this animal received 2 ccm. of broth culture of staphylococcus aureas in the knee-joint. With each infection there was only a slight local reaction. One hundredth day: Animal walks on limb with slight limp; knee allows free passive motion. Animal sacrificed. On opening the joint there is a small amount of thick mucous-like fluid; there are no adhesions in the joint. About the patella surface there is a zone of villi which when depressed show the cartilage to be undermined. About the periphery the femoral cartilage is roughened and has the appearance of fibrous tissue. The joint-capsule is reflected from the anterior surface of the femur at a lower level than normal. About the insertion of the cruciform ligaments there is a change in the cartilage similar to that seen at the patella margin.

Microscopical study. Sections were cut from the patella, femur, and tibia. The synovial membrane is thickened; there are numerous villi extending into the joint. The joint surface of the cartilage is normal except at the junction of the cartilage and the synovial membrane, where there is destruction of cartilage by granulation tissue. Extending from the epiphyseal marrow spaces into the under surface of the cartilage are numerous processes of granulation tissue.

Experiment No. 29. Injection 1 ccm. of a suspension of tubercle bacilli into the knee-joint cavity. Fifth day: Animal in good condition; knee swollen, tender, and hot; motion is limited. Twelfth day: Animal has lost weight; knee is held flexed, is hot and tender. Sixteenth day: Animal sacrificed. On opening the joint there was no excess of free fluid. The joint-capsule was thickened and adherent to the sides of the femoral condyles by a mass of granulation tissue. The synovial surface was partly covered by irregular areas of red, translucent tissue in which there were numerous small nodular elevations. The cartilage over the patella was normal. About the margin of the patella was a zone of granulation tissue. There were no adhesions between the femur and the patella. The lateral surface of the external condyle was denuded of cartilage almost to the edge of the patellar groove. There is destruction of cartilage in the intercondylar groove about the insertion of the cruciform ligaments. The space between the femur and tibia is filled with granulation tissue.

Microscopical study. Sections were cut from the patella, femur, and tibia. The

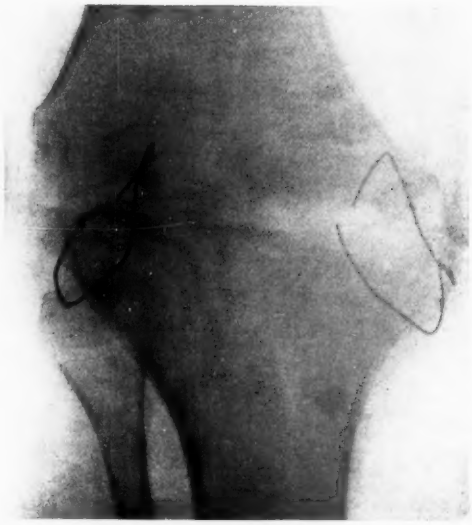


Fig. 27. Resection of the knee-joint in man, thirteen months after operation. Note that there is no bony union. There was no motion at the knee.

Fig. 28. Resection of the knee-joint in man, three years after operation. Note the union of bone.

synovial membrane is markedly thickened and shows an infiltration with lymphocytes and polymorphonuclear leucocytes. The joint cartilage is normal except at its margins, where there is cartilage destruction. The bone-marrow of the epiphysis shows very little inflammatory reaction. There are a few areas in which granulation tissue is invading the cartilage from beneath. On the anterior surface of the patella is a small nodule of new-formed bone. There is no tubercle formation.

Experiment No. 20. Injection 2 ccm. staphylococcus aureas into knee-joint cavity. Eleventh day: Joint not swollen; slightly tender; limb not used in walking; animal in good condition. Thirteenth day: Injected 2 ccm. of tubercle bacillus suspension into same knee-joint cavity. Seventeenth day: Knee slightly tender; slight heat; not used in walking. Twenty-fifth day: Animal in good condition; knee held flexed; slightly tender. Thirty-second day: Knee thickened, tender, and hot; not used and is held in acute flexion. Eightieth day: Limb held in right-angle flexion. Joint thickened; allows little motion. Animal sacrificed.

Microscopical study. Median longitudinal sections show the synovial membrane to be tremendously thickened. The joint cavity is much decreased in size. The joint-cartilage shows destructive changes throughout. The cartilage of the internal condyle is completely destroyed. This destruction is brought about by granulation tissue invading the cartilage from beneath and from the synovial membrane at its margins. In some cases the granulation tissue from the synovial membrane extends over the cartilage for a considerable distance. There is no tubercle formation.

Summary. In these experiments, in which bacteria were introduced directly into the joint cavity, characteristic pathological changes resulted. The joint changes in the experiments in which tubercle bacilli were used were the same as those observed in the experiments in which the staphylococcus was used. The extent of the joint changes and the general reaction to the infection varied widely in the different experiments.

Immediately after the introduction of the infectious agent into the joint cavity there

was a marked local reaction evidenced by swelling, heat, and tenderness. There was a fibropurulent exudate in the joint cavity, which produced adhesions between the capsule and the condyles, resulting in a marked diminution in the size of the joint cavity. The destruction of the joint-cartilage was always the result of absorption by granulation tissue. Granulation tissue arising from the proliferating synovial membrane destroyed the cartilage at its margin, and granulation tissue from the bone-marrow destroyed the cartilage from below.

GENERAL SUMMARY

From the experiments in which the joint cavity was infected with tubercle bacilli or staphylococci, or in which a slight injury was done the joint-cartilage, we are led to believe that any inflammatory process within a joint, which is of sufficient severity to result in the formation of granulation tissue, will destroy the joint-cartilages. The cartilage is absorbed at its margin by granulation tissue from the synovial membrane, and at its base by granulation tissue from the bone-marrow.

By the experiments in which the cartilage was removed by operation, or the joint partly excised, we have shown that ankylosis by bone is a slowly developing process which consists of the following stages: *First*, there is union by granulation tissue; *second*, there is union by dense fibrous tissue; *third*, there is a metaplasia of fibrous tissue into fibrocartilage and a direct transformation of this tissue into bone. The shortest period of time in which complete bony ankylosis was observed experimentally was one hundred and eighty days. That in man the duration of the process is equally prolonged is shown in Figs. 27 and 28.

The long duration of the process of osseous ankylosis, we believe, explains the following: After arthroplasty a joint may allow motion for some weeks and subsequently become stiff. Fractures of the epiphysis unite by bone slowly. It also suggests that the conclusion reached by certain investigators that the interposition of soft parts prevents bony ankylosis is misleading in that many of the experiments were of insufficient duration.

The long duration of the fibrous stage of ankylosis also shows conclusively that any method of arthroplasty should have as its object the prevention of fibrous ankylosis rather than bony ankylosis; also that the insertion of an irritative substance into a joint should be avoided.

We believe that the difference which exists between the epiphysis and diaphysis in the capacity for bone regeneration is explained by the fact that there is no periosteum on the epiphysis.

REFERENCES

1. Allison and Brooks. The Mobilization of Ankylosed Joints. Surg., Gynec. & Obst., 1913, vii, 645.
2. Hoffa, A. Orthop. Chir., 1902; Stuttgart: F. Enko, ed. iv, pp. 55–56.
3. Nichols and Richardson. Arthritis Deformans. J. Med. Research, 1909, xxi, 149.
4. Axhausen and Pels. Exp. Beitr. z. Genese d. arth. Deform. Deutsche Ztschr. f. Chir., cx.
5. Kroh, F. Exp. Arthritis Deformans. Deutsche Ztschr. f. Chir., 1909, xcix, 425.
6. Sumita. Arch. f. klin. Chir., 1913, xcix, 775.

IS THROMBO-ANGIITIS OBLITERANS AN INFECTIOUS DISEASE?

By LEO BUERGER, M. D., New York City
Instructor in Clinical Surgery, Columbia University; Associate Surgeon and Associate in Surgical Pathology, Mount Sinai Hospital; Visiting Surgeon Har Moriah Hospital

SINCE 1904 I have been collecting pathological material and clinical data on that interesting group of cases of presenile gangrene which have been described by the Germans under the name "endarteritis obliterans," and for which in May, 1908, before the Association of American Physicians, I proposed the term "thrombo-angiitis obliterans."[1] At that time my deductions were based on a study of the vessels in nineteen amputated limbs, but today I am able to draw my conclusions from a much larger number; namely, forty amputated limbs, two amputated forearms, and some twenty-five extirpated veins from eighteen cases of thrombo-angiitis afflicted with migrating phlebitis of the superficial veins.

With the rapid increase in the Jewish population of the city of New York during the last decade has come the opportunity of studying a disease which, curiously enough, seems to afflict this race almost exclusively, and particularly the immigrants or children of immigrants from Poland, Gallicia, and Russia. During the last eight years some two hundred cases have come under my observation. This large number, seen mostly in hospital and consultation practice, speaks eloquently for the frequency of its occurrence and for the importance of discovering the causative agent.

It would be superfluous to present a record of all those facts and observations that have been gathered by me from this large amount of material. I wish merely to call attention to the conclusions that I regard as significant from the standpoint of pathology and etiology. These may be briefly summarized in the statement that, in the light of clinical and pathological studies, we are warranted in thoroughly supporting the proposition that thrombo-angiitis obliterans is an infectious disease in which a specific type of organism is at work; and although it has not as yet been possible to demonstrate either bacteriologically or morphologically the presence of the offending agent, the pathological findings clearly indicate whither future studies should be directed in order that the causative factor may be discovered.

In order that the arguments in favor of such revolutionary views may be followed, it may be well to review briefly the conclusions reached in some of my earlier studies. In May, 1908, I maintained that the pathological pictures could be explained upon the theory that we were dealing with extensive thrombosis in arteries and veins followed by organization and canalization, and that the lesions in the vessels might be summarized as follows: Most of the larger arteries, and sometimes the veins as well, are obliterated over a large extent of their course. All stages in the occlusive change may occur in the various vessels of an extremity, or in the same vessel in different parts of its course. The closure of the vessels is affected by red obturating thrombi; these become organized, vascularized, and canalized. Recent red thrombosis may involve large portions of arteries or veins and is not secondary to the gangrenous process. It occurs even when no gangrene is present. In short, we are dealing with lesions of considerable extent, apparently initiated by the formation of occlusive thrombi, chiefly in arteries, but not confined to these, followed by organization or healing, with an attempt at the production of sufficient collateral circulation.

As for the cause of the thrombosis, my studies failed to reveal anything suggestive. The finding, however, of a peculiar type of histological picture in certain of the veins and arteries led me to believe that the same determining cause which leads to the thrombosis also evokes the changes in the media adventitia, and perivascular connective tissue; and, further, that although the mechanical conditions that obtain in the lower extremities and the arteriosclerotic changes

[1] Am. J. M. Sc., Oct., 1908.

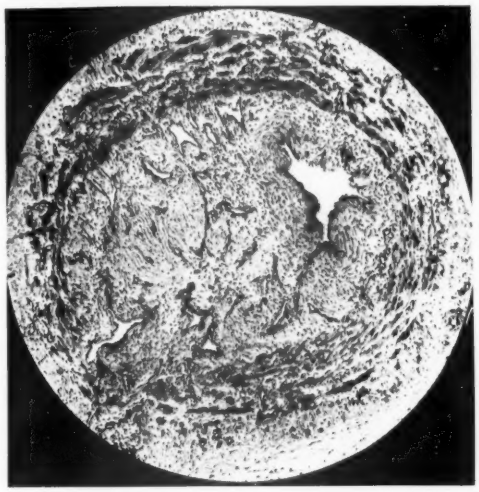


Fig. 1. "Old" type of occlusion in a deep vein; lumen occupied by vascularized dense connective tissue.

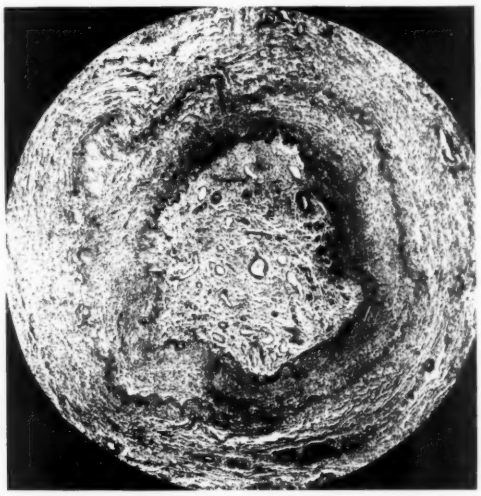


Fig. 2. Popliteal artery occluded by vascularized connective tissue, pigment, small vessels, and capillaries being features.

may be factors, some additional agent, be it toxic or otherwise, is at the same time responsible for the production of the periarteritis and the thrombosis.

Unfortunately, we are dealing with the vessels obtained by amputation, and it is extremely difficult to obtain material in the early or acute stages of the disease. When limbs are amputated, the disease is usually of long duration and the arteries and veins are already in the stage of organization. The presence of the acute and specific picture in two of the cases, however, was so suggestive as to lead to the supposition that *here* was the lesion in its earliest stage.

It was most gratifying, therefore, to learn that the subcutaneous veins of the upper and lower extremities may also be affected by the same disease. When, in the course of the observations, the association of migrating phlebitis of the superficial veins with the symptom-complex characteristic of the occlusion of the deep vessels was first noted, it appeared of no little moment to determine whether the newly discovered phenomenon was not a manifestation of the same malady. Collecting these cases, I was able to report, in 1909,[1] eleven patients who, at one time or another in the course of the disease, had suffered from thrombophlebitis involving the superficial veins of either the upper or lower extremities. From these investigations the following conclusions seemed warranted:

1. The disease thrombo-angiitis obliterans is often associated with thrombophlebitis of superficial veins of the arms and legs.

2. Certain peculiar cutaneous nodosities are characteristic manifestations in many of the cases.

3. The disease of the superficial veins may be subsidiary, or it may dominate the clinical picture. Objective signs referable to these vessels should be regarded as extremely suspicious marks of the synchronous development of thrombo-angiitis obliterans. In the presence of migrating phlebitis or cutaneous nodosities we should carefully search for evidence of thrombo-angiitis obliterans, in the form of pulseless vessels, erythromelia, blanching of the leg in the elevated posture, cold and blue toes, pain in the calf of the leg brought on by walking, and other typical phenomena.

4. Migrating thrombophlebitis may give no symptoms, the signs referable to the deep vessels being of most importance.

[1] International Clinics, 1909, pp. 85–106; and Mitt. a. d. Grenzgeb. d. Med. u. Chir., 1910, pp. 353–376.

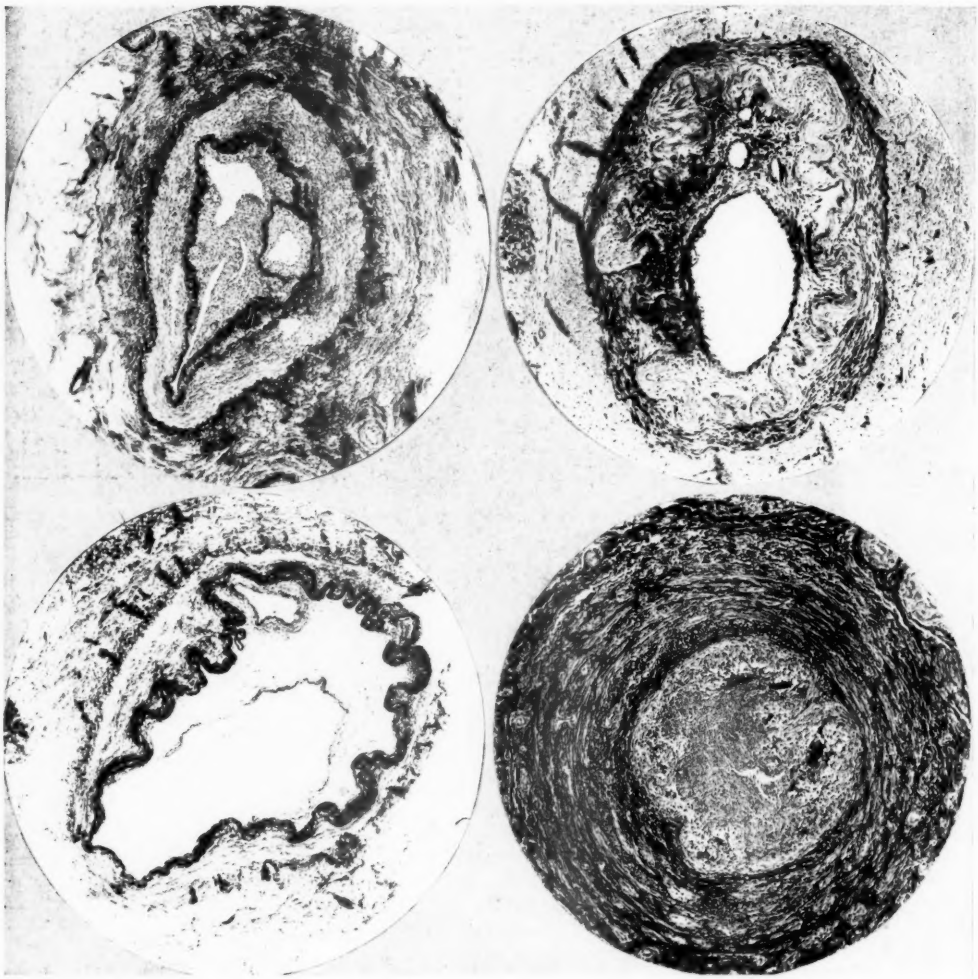


Fig. 3. Fig. 4.
Fig. 5. Fig. 6.

Fig. 3. "Old" occlusion of the fenestrated or cribriform type; large canalizing veins in fairly dense connective tissue filling the lumen of an artery.

Fig. 4. "Old" occlusion in artery simulating "endarteritis obliterans"; eccentrically situated large canalizing vessel (below) crowding rest of tissue to one side (above in the illustration).

Fig. 5. New lumen found in organized clot in vein simulating endarteritis obliterans (elastic tissue stain).

Fig. 6. Acute, early lesion with "miliary giant-cell foci" in periphery of clot filling lumen of deep vein.

5. Patients may suffer at one time from the migrating thrombophlebitis, at another from the progress of occlusive change in the deeper vessels.

6. Certain cases suggest the possibility that attacks of trouble in surface veins may occur simultaneously with similar exacerbations of disease in deep vessels of another limb.

7. The morbid process resulting in the production of cutaneous nodosities and thrombosed superficial veins is independent of

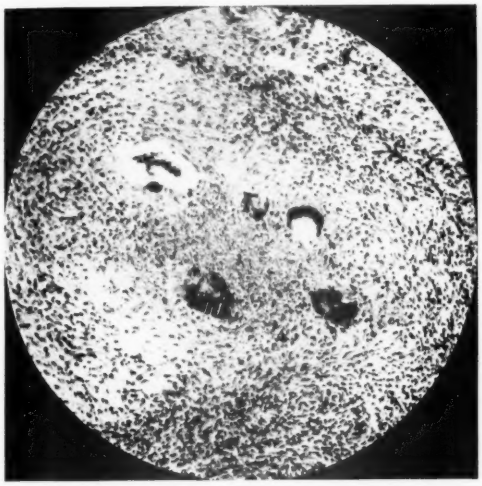


Fig. 7. Giant-cell focus of a daughter-canalizing vessel in obliterated artery; acute exacerbation in canalizing vessel.

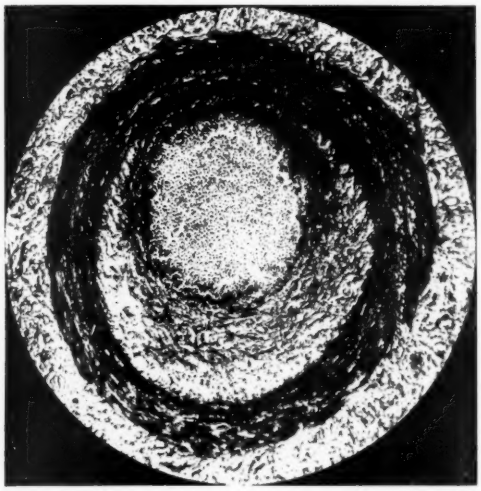


Fig. 8. Acute lesion in internal saphenous vein; above, purulent focus; below, remaining crescentic portion of lumen filled with organizing clot.

varicosities, of infections, or of trophic disorders in the territory which they drain.

8. The vessels of the upper extremity may be affected by the lesion thrombo-angiitis obliterans.

9. Thrombophlebitis in the arm and forearm should arouse our suspicions as regards involvement of the deep vessels of the legs.

10. Further studies should be directed toward solving the relationship between the two thrombotic lesions we have described.

Since 1909 I have been able to gather data on twelve additional cases in which the superficial veins were involved, and have brought the number of exsected veins to twenty-five. In these, both the acute and healed stages of the disease were found. From a consideration of the pathological picture the conclusion was reached that a specific characteristic lesion of thrombo-angiitis obliterans may affect the deep as well as the superficial vessels, and that it is from the lesions in the veins that we shall be able to gain access to material for investigation of the causative agent.

For the purpose of demonstrating the sequence of the various stages of the pathological process from its earliest obtainable stage up to the "healed" or obliterated connective-tissue stage, and in order to make clear the arguments in favor of my theory, it seems best to present a few selected histological pictures[1] in the way of illustration. In these I shall endeavor to point out the general appearances of the old lesions in the deep vessels; the acute type of lesion in the deep veins and arteries; the lesions as seen in the veins under the skin — and how these latter are identical with the lesions of thrombo-angiitis obliterans; and, finally, why the findings point so suggestively to the presence of some microbial agent although none such has as yet been revealed.

Let us review the pathological changes in the obliterated vessels in the sequence in which we have met them in the course of our studies, beginning with the most common lesion in the "healed" stage, as it is encountered in the majority of the diseased vessels, removed from an amputated arm or leg.

Such vessels, be they arteries or veins, are filled with connective tissue (Fig. 1) bearing numerous canalizing vessels (Fig. 2), often some pigment of blood origin, not infrequently presenting a cribriform appearance in the freshly cut surface of a transverse section

[1]For some of the photomicrographs I am indebted to Dr. F. S. Mandlebaum, pathologist of the Mount Sinai Hospital; for others, to Mr. Dunn, of the Cornell University Photograph Department.

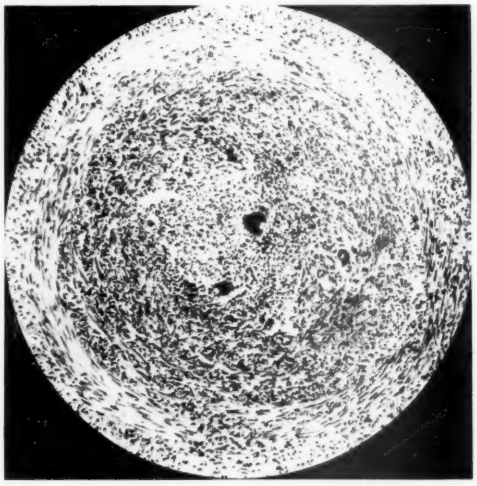


Fig. 9. Acute lesion in superficial vein; media infiltrated giant-cell focus.

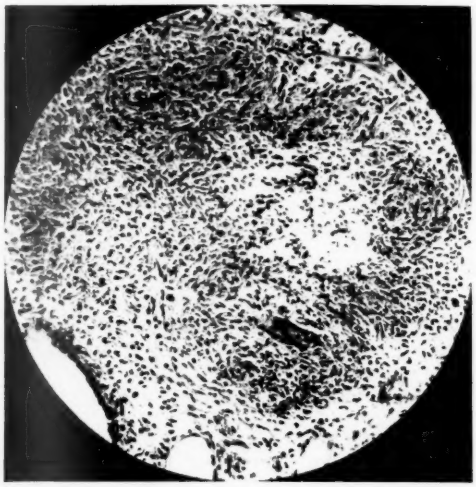


Fig. 10. Later stage in "acute lesion," simulating miliary tubercle; endothelioid cells and giant cells surrounding focus of disintegrating leucocytes.

(Fig. 3). That the obliterating lesion should have been misinterpreted and regarded as an obliterative *endarteritis* is not surprising when we look at the pictures afforded by the artery seen in Fig. 4, where a large canalizing vessel simulates a narrowed lumen and crowds the rest of the organized clot to one side. Such a vessel may be seen to divide, if its course be followed in serial sections, and the manner of its formation distinctly seen. In Fig. 5, also, there is a vein in which the picture of an endarteritis is mimicked.

All stages of the process, from the finished organized product back to the early thrombotic lesions where arteries and veins are filled with red clot, were studied in the forty amputated legs and two amputated arms. For our purpose here, it will suffice to call attention to the earliest or "acute" stage of the disease, as we were able to discover it in the vessels of but two of the forty amputated legs.

In many vessels the wall is diffusely infiltrated with leucocytes, more marked in some places than in others, and the lumen completely occluded by red clot in which certain characteristic foci, elsewhere referred to as "miliary giant-cell foci," make a striking picture (Fig. 6). When these were first encountered in our studies their significance was not understood, except in so far as they seemed unique and specific for thrombo-angiitis, not having been seen in thrombosis due to other causes.

More recent investigations have clarified our notions, so that to-day a satisfactory explanation can be given for these very peculiar and seemingly "specific" morphological alterations. A change even earlier than this was sometimes found in the deep vessels, namely, foci of pus-cells in the periphery of the red clot, such areas being the precursors of the "miliary giant-cell foci" that resemble miliary tubercles. The suspicion that we were dealing with some specific microbial process was already aroused when the peculiar appearances in deep vessels were noted, not only because such changes had never been seen elsewhere, but also because the typical foci could even be discovered in "daughter" canalizing vessels of arteries that were already in the healing stage. Fig. 7 shows such a specific focus taken from a canalizing vessel that was evidently the seat of an "exacerbation" or "recrudescence" of the disease thrombo-angiitis obliterans.

Material, however, whose source is confined to amputated members, must needs

be difficult to obtain, for seldom will it be our fortune to see the early lesions. Amputation is naturally only considered after the disease has progressed for many months or even years, when the patients are suffering from the mechanical phenomena due to obstructed inadequate vessels rather than from the acute stage of the disease.

It was, therefore, a happy circumstance that the superficial subcutaneous veins of the arms and legs were found to be involved by what has elsewhere[1] been termed an associated migrating phlebitis. From this source we were able to obtain adequate material for the establishment of the facts that the veins under the skin may be the seat of thrombo-angiitis obliterans; that the acute type of lesion in the superficial veins gives a specific picture similar to that in the deep vessels, and that the development of the lesion in its incipient stages can be studied, enabling us to explain the production of those bizarre appearances heretofore so inexplicable in their nature.

Let us turn to Fig. 8, in which a tributary of the internal saphenous vein presents a purulent focus in a portion of the obturating clot: The rest of the clot is composed of red cells, some white cells, and fibrin already in the process of organization by capillary ingrowth. The purulent focus can be seen to be invaded by leucocytes from the media and adventitia (Fig. 9) and certainly does not represent merely agglutinated leucocytes derived from the intravascular blood.

Such foci vary in size, and it can be definitely established that their growth occurs by virtue of the immigration of leucocytes. Next in the life history of the lesion comes an attempt at healing these suppurative areas, and in this process are found those characteristic and peculiar pictures elsewhere called "miliary giant-cell foci." Evidently the microbial agent, toxin or whatever it may be, is concentrated especially in these areas.

Here it is instrumental in attracting leucocytes into the formation of miliary abscesses, and it may exert a more protracted force or influence in preventing that orderly and typical organizing process that is so characteristic and so well known. Instead of the rapid ingrowth of angioblasts with the production of young capillary sprouts, the vessel-forming cells (angioblasts) seem to lose their power of purposeful penetration into the suppurative areas — grow wild, as it were, become distorted and atypical, and arrange themselves along the periphery of the foci in the form of cells that we recognize as "endothelioid." Often they can be seen penetrating for a considerable distance into the leucocytic focus — fraying out, never able, at this stage, to produce capillaries. On the other hand, they do frequently terminate in the production of the typical giant-cells. This is the earliest stage in the attempt at organizing or healing these miliary foci.

At the same time, the typical successful organizing process may be found going on in other parts of the lumen of a vessel. Thus, in Fig. 8, the crescentic area adjacent to the miliary focus is occupied by red clot and fibrin, successfully and normally organized by angioblasts.

Later, as the giant-cells arrange themselves about the periphery of the focus and penetrate it to a certain extent (Fig. 9), the leucocytes disintegrate, and finally a tubercle-like formation (Fig. 10) is the result. The purulent products become absorbed, and the focus becomes converted into connective tissue.

The giant-cells and endothelioid cells are but the expression of abortive attempts on the part of the angioblasts at organizing or healing a focus which is infectious. The true purpose of the vessel-forming cell (angioblasts), at times so beautifully illustrated in other parts of the same vessel lumen, is thwarted.

Later, all vestiges of the acute lesion disappear; the occluding thrombus becomes converted into vascularized connective tissue; the leucocytes and wandering cells disappear from the media, adventitia, and perivascular connective tissue, an obliterated, canalized, and adherent vessel being left as the final product.

Such, then, are the acute lesions in the veins. They bespeak the presence of a microbial agent that must be sought for in the peculiar characteristic foci previously

[1] Loc. cit.

described. Up to the present time, all our attempts at detecting the causative agent have been futile.

Spirochætæ, tubercle bacilli, the ordinary pyogenic organisms, have been carefully looked for in cultures, in microscopic sections, and by inoculation methods, without result. However, the search must not be given up, since but relatively little of the "acute" material has as yet been available for study.

Although, in this rapid review of a subject which still presents so many mooted points for investigation, it has been impossible to give all the details which support the theory advanced, it is hoped that a vigorous plea in favor of the correctness of the following points has been made:

First, that thrombo-angiitis obliterans is a disease in which an acute inflammatory lesion and occlusive thrombosis of arteries and veins are the characteristic lesions.

Second, that from the mechanical point of view and from the standpoint of symptomatology, the thrombotic occlusion is the most important phenomenon.

Third, that the thrombosis is probably preceded, and certainly accompanied, by an acute inflammatory or exudative stage.

Fourth, that the lesion involves deep veins in about 40 per cent, and the superficial veins of the upper and lower extremity in 20 per cent, of the cases.

Fifth, that recent investigations of the veins show that the acute lesions in the superficial vessels and then deep vessels are identical.

Sixth, that the histological changes in the veins point to the existence of an infectious process.

Seventh, that we believe that future studies should be directed toward the discovery of the causative agent in specimens cut out from the superficial veins when they are the seat of the acute thrombophlebitis. In this way it is hoped that the etiology of the disease may soon become revealed.

FORWARD FIXATION OF THE CERVIX AS A PREDISPOSING CAUSE OF SOME RETRODEVIATIONS OF THE UTERUS, AND AN OPERATION FOR ITS RELEASE[1]

By EDWARD REYNOLDS, M. D., Boston

PROGRESS in practical matters is usually inaugurated by prior work on the theoretical considerations which underlie it. This brief paper will therefore contain a statement of the views as to the support of the uterus which have guided me of late years, my conception of the anatomy of the abnormal condition which I believe is a predisposing cause in many cases of the retrodeviations, and a description of the operative procedure by which I am in the habit of correcting it. I feel bound, however, to say here that no one can be better aware than I am that under the limitations of time imposed upon us most of the statements which I am about to make are little more than personal assertions, nor indeed that my views are for the most part merely the result of personal clinical observations which cannot be accepted by any one else as proof of their correctness. These observations have, however, extended over so long a period of time, and have to the best of my belief been conducted in so skeptical a spirit, i. e., with so consistent an effort at the attitude of scientific doubt, that I am personally very strongly convinced of their correctness. The practical results which have followed their adoption have, moreover, seemed to me to be so good that I am quite content to pursue the method in my personal work and am quite convinced that in the process of time they will prevail.

The uterus is sustained in its position in the pelvis by the resultant of the action of a great number of unstriped muscular fibers

[1] Read before the American Gynecological Society, Boston, May 21, 1914.

which are partly disseminated throughout the pelvic connective tissue and partly aggregated into bundles lying within reflexions of the peritoneum which have long been falsely called uterine ligaments. The gynecological profession has been extremely slow in accepting this advance of knowledge in regard to the composition of the uterine ligaments, falsely so called, but a search through the anatomical literature of the last ten years will convince any one that among anatomists this is standard knowledge, and I think that no gynecologist can long watch the behavior of these tissues as he cuts through them during operation without becoming convinced of their retractile power; i. e., of their muscular action. The chief bundles of such fiber are distributed along the course of the ovarian and uterine arteries, to which we must add the round ligaments; and it must not be forgotten that lesser quantities of unstriped muscular fiber are distributed throughout the entire body of the broad ligament.

My own observations during recent years have convinced me more and more strongly that study of the pathologic spasms of these muscular structures is opening up a whole new field in gynecology, more especially in the relation of pelvic lesions to neurasthenia and the production of pain; but a reference to this is not my present purpose, which is the influence of these structures on the production and relief of the retrodeviations.

The uterus as a whole is then sustained by elastic (muscular) tissue, and the cervix is the only part of it which is attached to the bones, or to the firm connective tissues over them, by inelastic connective tissue, this attachment being the extremely strong and unyielding anterior vaginal wall with its firm attachments to the pubic arch, and the median Y-shaped ligament[1] first described by Goffe which extends from the cervicovaginal attachment to the connective tissue above the pubic arch on each side of the urethra.

The anomaly known as anteflexion of the cervix is not separated by any sharp line from the normal slight forward curve of the organ, cases being found in every degree of variation from the normal, through the high normal and the slightly pathological, into the highest degree of anteflexion. It is now generally conceded that this abnormality is an arrest of development; but I think it is not generally understood that this arrest of development is never confined to the cervix alone but necessarily includes also a short anterior vaginal wall, i. e., an underdevelopment of this firm structure and of Goffe's ligament, by which the vaginal cervix is held in forward fixation close under the pubic arch.

This shortened attachment holds the *vaginal portion* of the anteflexed cervix firmly forward, while the *supravaginal* cervix is at the same time steadied from side to side by the powerful muscular action of the lower portions of the broad ligaments along the uterine arteries, and drawn backward by the almost equally powerful uterosacrals. The *fundus* in its turn is held forward by the disseminated muscular fibers in the upper parts of the broad ligaments and by the occasional action of the round ligaments. Such a uterus has an intrinsic angle in its shape situated at about the internal os; but with the vaginal cervix fixed forward and with the fibers in the vicinity of the round ligaments drawing the fundus forward, the action of the muscular uterosacrals in drawing the middle of the organ back tends constantly to an exaggeration of this angle. With the onset of the catamenial congestion the uterine walls engorge with blood, and under primary hydrostatic laws the organ tends to resume its normal shape; i. e., to efface any increase of angulation due to the action of these muscles.[2] Under these conditions, with the cervix fixed forward and with the uterus trying to straighten itself, the fundus would of necessity turn backward were it not for the muscular action of the round ligaments and the unstriped fibers which accompany them. If, then, at any moment this action relaxes, even temporarily, the fundus must of necessity move backward; that is, in other words, with the cervix, the lower pole of the organ, fixed forward to an abnormal degree, any straight-

[1] It would be more exactly described as a sheet of fascia.

[2] Unfortunately these muscles, also, with the onset of the precatamenial congestion tend to increase their action, to pass into more or less well-defined spasm; and the result of these antagonizing forces is backache and usually dysmenorrhœa; but this only in passing—I am here concerned only with the production of the retrodeviations.

ening of the organ under the influence of the menstrual congestion of necessity throws the fundus backward in some degree, though not always enough to constitute a retroversion. But we have long known that the moment the fundus moves backward even in a small degree it receives the effect of the general intra-abdominal force on its anterior face and therefore tends to move farther backward; i. e., to assume the first degree of retroversion, which then tends to become progressive.

I believe that in this mechanism we have an inherent tendency, a predisposition towards retroversion, which in the constantly recurring physiological congestions from one and another cause is extremely likely to be converted into a fact, an actual retroversion, at some time or another during the life of a woman having such tendency. My first point, then, is that owing to the underdevelopment (the undue shortness of the anterior attachments of the cervix which are characteristic of anteflexion of that organ), women with anteflexion of the cervix have a tendency toward retroversion, as the result of slight accidental causes which would probably not produce that retroversion in the case of women in whom the lower uterine pole was in a normal position.

I had reached a tentative conclusion to this effect some five or six years ago, and since that time under continued observation I have, with the exception of a class to be spoken of shortly, rarely seen a retroversion of the uterus in which the amount of anteflexion of the cervix was not at least high normal, or beyond the normal.

The class of which this is not true consists of those cases in which the uterus is dragged backward by the weight of a heavy new-growth or by the posterior adhesions of an infected salpinx.

I have now come to believe that outside of this class of cases, and with of course possible rare exceptions, the retrodeviations do not ordinarily occur except in women in whom the cervix has more than a normal degree of forward fixation.

Time does not permit the discussion of all the varieties of the retrodeviations in this connection, but I may say in answer to a question which would at once present itself that when a descensus of the uterus occurs as the result of post-obstetric subinvolution and lack of perineal support, I believe that if the cervix is normally movable we get a descensus which eventually becomes a prolapse, but that under the same circumstances in a woman who is the subject of an anteflexion of the cervix, i. e., of a forward fixation of the cervix, the descensus is converted into a retroversion by the fact that the fundus descends while the cervix is still held high. In all cases of forward fixation there is a tendency to retroversion because the cervix is held forward while the fundus is movable.

The diagnosis of forward fixation is best obtained by adding to the ordinary observation of the shape of the uterus, of the direction of the vaginal cervix, and of the presentation of the os, a further estimation of the mobility of the cervix, which is obtained by the attempt to move it upward and backward with the finger or with a double hook.

A short series of observations on women, some of whom have, and some of whom have not, the abnormality commonly called anteflexion, will establish in any one's mind the normal mobility of the cervix and the degree of forward fixation which may be considered an abnormality; and will, I think, further establish the comparative frequency of a degree of this abnormality which is mechanically effective.

The operative method which I have now come to adopt as a matter of routine in all cases of the operative treatment of retrodeviations which show any considerable degree of forward fixation of the cervix, is to precede the abdominal treatment of the retrodeviation by a method of vaginal release of the forward fixation which I have already once described to you, but which I may briefly recapitulate here, more especially as I think I have decidedly improved my technique since the date of the former paper.[1]

After a preliminary dilatation and curettage the vaginal wall is seized with forceps

[1] Anteflexion of the Cervix and Spasm of the Uterine Ligaments in Relation to Retroversion, Dysmenorrhœa, and Sterility. Surg., Gynec. & Obst., 1911, xiii, 17.

immediately in front of the cervix and divided with scissors throughout its thickness, a narrow transverse strip being removed. The length of this transverse incision must vary somewhat with the size of the individual vagina, but it should ordinarily be just sufficient to admit the operator's index finger. The anterior lip of the cervix is then seized with volsellum forceps, one blade of which enters the vaginal wound, while the other lies within the cervical canal. Traction downward and backward brings Goffe's ligament into view. This is also divided transversely with scissors over the whole width of the transverse wound, so exposing the loose connective tissue between the cervix and bladder. All the tissues in front of the cervix are then separated from it with the index finger passed through the wound up to or slightly above the level of the internal os, and as far out to either side as the finger can conveniently reach, thus freeing the anterior surface of the broad ligaments as well as the cervix. The transverse wound in the vagina is then brought together by a transverse running suture, thus elongating the anterior vaginal wall. If the transverse wound is too wide, some narrowing of the vagina may result; but if this is watched for, it can be avoided easily by a slight variation of the suture, i. e., by bringing the lateral extremities of the cut together in the reverse direction (longitudinally to the vagina instead of transversely). During the first stage of this little operation there is frequently free bleeding, but it comes only from the cut edges of the vaginal wall; and if the division of the deeper tissues is done with the finger, all bleeding will be controlled by the sutures. It is often well to make sure that the cavity is clear of clot before closing it, either by the use of a sponge or by irrigation. At the conclusion of this stage of the operation the cervix will be found to have become freely movable and to have receded into the posterior cul-de-sac, but since it is still crooked and the os still looks forward it is well in most cases to complete the operation by a discision of the posterior lip. This I formerly did after the method of E. C. Dudley; but experience has shown that this method leads to a subsequent eversion of the cervical mucous membrane in so large a proportion of cases that instead of making a simple median incision I now remove a lozenge-shaped portion of the posterior lip by four cuts of the scissors. The first two cuts divide the edge of the os at the same point in the median line, but at the other end are from a quarter to a third of an inch apart; the next two cuts start at the extremities of the other two and meet in the median line, thus removing the lozenge. The upper apex of the lozenge should be externally at or nearly at the vaginocervical junction and internally should reach almost to the level of the angle of flexion in the individual case. Two sutures longitudinal to the vagina, one on either side of the cut, then bring the longitudinal points of the lozenge together at the cervicovaginal junction, thus shortening the posterior lip of the cervix and yielding a straight uterine canal. After the recovery of the patient from ether, the lower pole of the uterus will now be drawn strongly backward and upward by the unopposed action of the uterosacrals, and the application of a suspension, or of any of the standard round-ligament operations to the upper pole, completes the operation. There is now everything to keep the fundus forward and no opposing force to turn it backward.

Since the adoption of this procedure my percentage of failures after operations for the retrodeviations has diminished almost to the vanishing point, and I have come to feel that with this addition almost any one of the accepted operations is as good as any other.

I think that if you will treat my two main points—that abnormal anterior fixation of the cervix is the chief predisposing cause of the posterior deviations of the fundus, and that the operative release of this forward fixation of the cervix is a most potent addition to our means of combating such retroversions as need operative treatment—as hypotheses which are worthy of submission to observation and experimental use in your own daily work, you will soon be forced to the point of accepting them as established to your content, as they already are to mine.

A CRITICAL STUDY OF INTESTINAL STASIS, INCLUDING NEW OBSERVATIONS AND CONCLUSIONS RESPECTING THE CAUSES OF ILEAL STASIS [1]

By JAMES T. CASE, M. D., Battle Creek, Michigan
Assistant Surgeon and Röntgenologist to the Battle Creek (Michigan) Sanitarium; Röntgenologist to St. Luke's Hospital and to Cook County Hospital, Chicago; Lecturer on Röntgenology, Northwestern University Medical School, Chicago

WHILE Bouchard and Metchnikoff first furnished a rational explanation of the evil effects of intestinal stasis, it was Lane who first actually demonstrated these ill-effects by the good results of radical treatment. Whatever opinions may be reached by surgeons and internists regarding Lane's methods of dealing with alimentary toxæmia due to stasis in the intestine, the fact must be recognized that stasis does exist in a large number of cases, and that this stasis is sooner or later productive of far-reaching effects.

Not everyone who has intestinal stasis exhibits symptoms of alimentary toxæmia. Whether or not symptoms appear depends upon the integrity and functional capacity of the vital defenses of the body which normally deal with the products of intestinal putrefaction. In some cases, the defensive processes are able to destroy and eliminate even large quantities of putrefactive products; and intestinal putrefaction may exist to a marked degree and yet the patient show no signs of intestinal toxæmia. This fact is well known, of course, and attention is called to it here only for the purpose of emphasis.

As urged above, the fact of the common occurrence of intestinal stasis must be recognized and its importance conceded. The essential theme in Lane's teachings relates not so much to kinks or colectomies or short-circuitings as to the danger of continued stasis in the drainage system and the necessity of doing something, medically or surgically, to relieve it. Great credit is due this remarkable surgeon for the wave of interest in intestinal stasis which has swept over England and America, as evinced by the voluminous discussions which have been called forth in recent times, over this subject, which, as Keith puts it, is still but "a child of our ignorance." Pathologists, chemists, and bacteriologists have discussed the manner in which the poisons are formed and how they affect the body. Apparently it is not the poisons themselves which chiefly concern us, but the failure of the defenses of the body which should be constantly active against these poisons. Is it not, therefore, the rational thing to discourage the formation of the poisons in every possible manner, particularly through lessening the sojourn in the intestine of the material from which the poisons are formed?

The relation of pyorrhœa alveolaris and other forms of mouth infection to infectious processes within the bowel has been well established. The recent debate on alimentary toxæmia before the Royal Society of Medicine seems to make it clear that much of the bacteriological and biochemical work which has been published concerning the flora of the large intestine and their poisonous products needs further revision. The consensus of opinion seems to be that the poisons of alimentary toxæmia may, in many instances, be chemical protein derivatives of comparatively simple formulæ. There is evidently a certain relation between alimentary toxæmia and diseases of the eye, certain skin manifestations, and various other constitutional symptoms. This is generally accepted. The part of the subject still under controversy relates to peritoneal bands and their relation to kinks, intestinal stagnation, increased putrefaction, increased formation of poisons, etc. As to the cause of these bands, there is a wide divergence of opinion. The X-ray evidence which has been brought forward in support of the stasis due to these supposed kinks needs careful inquiry concerning certain sources of error, to which attention will be called later.

Through my institutional connections—the Battle Creek (Michigan) Sanitarium and

[1] Read by invitation before the New York Academy of Medicine, Annual Meeting, January 15, 1914.

St. Luke's Hospital, Chicago—unusual opportunities have been afforded me for the röntgenologic study of intestinal stasis. This opportunity has been especially rich in the surgical clinic of the Battle Creek Sanitarium and Hospital.

About two years ago the tentative rule was made that every case for which laparotomy was recommended should be subjected to a thoroughgoing röntgenologic examination before being sent to the operating room. These examinations were ordered, not only for the purpose of gaining all possible information regarding the pathological features of the individual case, but also for the purpose of checking up the conditions which, according to the röntgenologic examination, appeared to be normal, and also to check up the röntgenologic appearance of parts which, at operation, were found normal.

After the first few months of this temporary rule for routine X-ray examination before laparotomy, the results in the way of help to the surgeon, and especially in connection with the problems of intestinal stasis, have warranted the continuance of this rule. At the present time, with the exception of cases of acute appendicitis and ulcerations of the stomach or bowel where perforation seems imminent, practically every case for laparotomy is referred to the röntgen examining room prior to operation. Out of an experience covering bismuth-meal examinations of approximately three thousand cases, studied both after the ingestion of a meal and during and following the injection of a bismuth enema, I have had the opportunity to follow a large number to the operating table. Not only have the X-ray findings been checked up by the report from the operating room, but the röntgenologist has made it a point to be present as one of the assisting surgeons at as many of the laparotomies as possible. Thanks to this opportunity, I have accumulated a large amount of data concerning various portions of the alimentary tract which otherwise would not have been available. Inasmuch as many of the patients were operated on for gastric, gall-bladder, uterine, and other abdominal and pelvic conditions, often not associated with intestinal stasis, it was extremely interesting to study the operative findings relating to kinks and torsions of the ileum and colon in connection with the motor function of the bowel, and particularly to note the frequency with which adhesions of the terminal ileum and colon were present in cases where, from the bismuth-meal examination or other clinical means of investigation, intestinal stasis had not been suspected, and in which there was no reason to believe the existence of ileal stasis. Relatively few of the patients were operated on directly for the relief of intestinal stasis.

In the experience of my colleagues and myself, it is with comparative rarity that radical surgery is necessary or profitable in dealing with intestinal stasis. Indeed, Dr. J. H. Kellogg, chief surgeon, has stated it as his belief that in scarcely more than one case of alimentary toxæmia in a hundred is short-circuiting with or without colectomy a warrantable operation.

Certainly there are exceptional cases in which dietetic and other non-surgical means have been tried thoroughly, and where short-circuiting, especially when an artificial ileocolic valve is made, has resulted in almost marvelous improvement. But the real pernicious stasis, the intestinal stagnation which is really damaging, it seems to us, is not colonic stasis, but ileal stasis. The early work of Lane dwelt more upon the stasis in the colon, but within the last four or five years his efforts have been focused on ileal stasis, and he agrees that it is of far greater importance than colonic stasis. Granting for the moment that the stagnation in the terminal ileum is due to adhesions about the terminal ileum, cæcum, or appendix, short-circuiting does not permanently relieve this ileal stasis unless a new ileocolic valve is made to act as a guard against the reflux of the contents of the colon back into the small intestine. In every case where I have made an examination with the X-ray, following the short-circuiting operation, I have observed retrograde peristalsis in the colon. In many of these cases there was also a reflux of colonic contents through the anastomotic opening into the small intestine, and the resulting stasis in the small intestine converted the terminal ileum into a

veritable colon; so that the patient, instead of having a colon five feet long, possessed a "colon" of indefinite length. In some such cases I have seen the terminal ileum having the caliber of the colon itself, so that when examined with the X-ray it was not easy to differentiate ileum from colon.

The chief purpose of this paper is to review the conditions which have thus far been advanced as causes of ileal stasis, and to lay emphasis upon a new cause of ileal stasis to which I first called attention in 1909.

Leaving out of consideration tuberculous and malignant disease in the neighborhood of the ileocæcal valve, there are, it seems to me, three efficient causes of ileal stasis.

The first cause, as suggested by Lane and later demonstrated röntgenologically by Jordan, consists in adhesions of the terminal ileum. Lane considered the ileal adhesions and stasis both secondary to stasis in the large bowel, giving rise to overloading of the cæcum and obstruction of the ileal effluent either by an acquired mesentery, an appendix hitching it up, or by simple stasis. But the acquired origin of the bands which Lane believes obstruct the ileum is questionable. According to Keith, during the third, fourth, and fifth months of fœtal life, a profuse, adhesive process sets in,— a "regulated, embryological peritonitis,"— which leads to the cohesion of mesenteries and viscera to the posterior wall of the abdomen, probably the adaptation to the upright posture. The extent of this process is extremely variable. Keith states that in about one newly born child in every ten the process of adhesions will be found to have bound the mesentery of the lower part of the ileum to the iliac fossa, giving the appearances to which kinking of the ileum is attributed. These adhesions may become so extensive as to give rise to the so-called Jacksonian membrane. Keith recognizes, however, that all peritoneal adhesions in the ileocæcal region are not embryological and normal, but that occasionally in adults there are found adhesion bands which are not seen in a child at birth. These may properly be considered possible causes of ileal stasis. The majority of the adhesions, however, are in reality mere expressions of a normal and healthy fœtal process. This view of the matter has also been suggested by C. H. Mayo, Eastman, and others in America.

Ileal kinks are often found accidentally at operation, and, since they may vary within certain normal bounds, in cases where their presence has been entirely unsuspected, may we not properly inquire into the propriety of surgical treatment of these adhesion bands thus accidentally found, unless by previous clinical examination (particularly by means of the X-ray) stasis has been found to occur proximal to the so-called kink? Where obstructing kinks have been found, there was (1) a dilatation of the ileum proximal to the kink — not proximal to the ileocolic valve; (2) delay in the ileum beyond the nine or ten hours considered the limit of its normal emptying time; and (3) the stasis has occurred, as above noted, proximal to the kink — not proximal to the ileocolic junction.

Through the train of circumstances related earlier in this paper, I have examined many cases of ileal stasis which have come to operation (uterine tumors, gall-stones, gastric or duodenal ulcer, as well as some extreme cases where the operation was done for the relief of the stasis) where no adhesions were found about the terminal ileum.

Hence we must conclude that (*a*) there are certain forms of obstructing ileal kinks; but (*b*) there are numerous other cases which have come to operation for various causes, in which kinks have been found, where a carefully conducted X-ray examination has shown the absence of ileal stasis and where there were no other clinical evidences upon which to base a belief that ileal stasis existed. (*c*) There has been another class of cases in which ileal stasis existed and no adhesions have been found. Study of these cases has led to the conclusion that a large proportion of ileal stasis is due, not to kinking or adhesions of the terminal ileum, but to incompetency of the ileocolic valve, or to spasm of the ileocæcal sphincteric mechanism, or to a combination of these two factors.

2. Ileocæcal sphincter spasm as a cause of ileal stasis, I find, was suggested as long ago as 1908 by A. F. Hertz. In September, 1912, before the American Röntgen Ray Society,

Fig. 1. Lane's kink of the ileum. Röntgenogram twenty-four hours following the bismuth meal. The ileocæcal valve was incompetent. The behavior of this case suggests that the Lane's kink was merely an incident, and that the ileocæcal valve incompetency is the real cause of the stasis.

Fig. 2. Lane's kink of the ileum, associated with adhesions of the appendix. Röntgenogram twelve hours post-cibum. Note the greatest distention of the ileum (*b*) is *distal* to the kink. The ileocæcal valve was incompetent. The arrows marked (*a*) point to the appendix, which lies across the ileum and is adherent to it.

unaware of the work of Hertz on this point, I suggested that many cases of ileal stasis were due to spasm of the ileocæcal sphincter. As part of his contribution to the discussion of alimentary toxæmia before the Royal Society of Medicine in the spring of 1913, Hertz again suggests that ileal stasis may be caused by spasm of the ileocæcal sphincter.

In man, according to Keith, the musculature of the terminal portion of the ileum for the extent of nearly four inches above the ileocæcal valve, is endowed with a special tonic function, whereby it serves as a sphincter for the terminal foot of ileum. Keith originally suggested that the function of the sphincter was to assist in preventing the contents of the ileum from passing too rapidly into the cæcum. Others thought that its function was to act as a barrier against the regurgitation of the contents of the cæcum back into the ileum. Doubtless both functions are active, although the principal influence against the reflux of colonic contents is the muscular action of the ileocæcal valve when it is competent.

The ileocolic junction, then, consists of two mechanisms: one, the valve mechanism, which mechanically prevents a reflux of the colon contents back into the ileum; the other, the ileocæcal sphincteric mechanism which controls the rate of passage of the contents of the terminal ileum into the cæcum, and probably also assists in guarding against regurgitation of cæcal contents.

Following a bismuth meal, at least an hour elapses between the arrival of the first bismuth-mixed chyme at the end of the ileum and the passage of any appreciable quantity into the cæcum; and four or five hours, or more, after the last portion of the bismuth meal has left the stomach, the terminal ileum still contains bismuth. In other words, there normally occurs in the lower end of the ileum a delay where the chyme remains undergoing digestion for a longer period than in

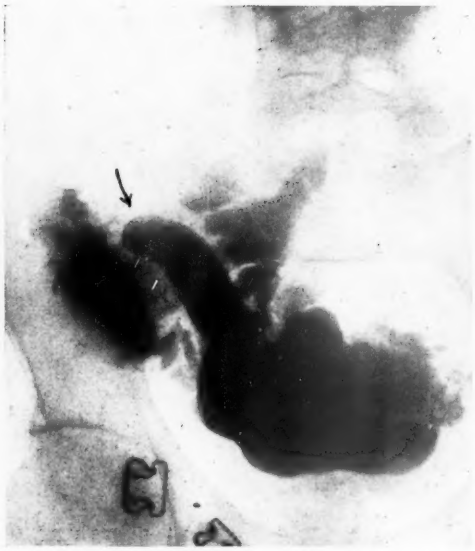


Fig. 3. Röntgenogram eight hours post-cibum, showing the terminal ileum widely filled and a trace in the cæcum. The appearance of the terminal ileum just proximal to the ileocæcal valve is what the writer considers characteristic of spasm of the ileocæcal sphincteric mechanism.

Fig. 4. Röntgenogram twelve hours post-cibum, showing marked stasis in the terminal ileum with an apparent ileal kink at the arrow (*a*) about three inches from the ileocæcal valve. The conical appearance of the terminal ileum at (*b*) just proximal to the ileocæcal valve is characteristic of ileocæcal valve incompetency, and when present one may prophesy that the ileocæcal valve will be incompetent to the enema. No kink of the ileum was found in this case, but the ileocæcal valve was markedly incompetent.

the stomach. According to Hertz, a certain amount of ileal delay is thus "a normal, physiological condition of the utmost importance for adequate digestion."

The behavior of certain striking cases which have passed under our röntgenological and surgical observation strongly supports the idea that the normal ileal retention is increased in all conditions leading to spasm, probably most marked in acute appendicitis, less marked in chronic appendicitis. It is probable that other conditions, perhaps even adhesions of the terminal ileum, may also prolong the retention which, up to a certain degree, is normal in the terminal ileum.

3. As a new and additional cause of ileal stasis, I have suggested incompetency of the ileocolic valve. Kellogg, Groedel, Dietlin, Rieder, and others have since agreed on the importance of recognizing this condition.

In 1909, I began to notice the frequency with which the bismuth enema passed beyond the ileocolic valve. Looking back over our statistics, I find this percentage very constant, about one out of every six gastro-intestinal cases showing incompetency of the valve. In 1911, I demonstrated röntgenograms showing incompetency of the ileocolic valve before the Gesellschaft für innere Medizin, Vienna, and shortly after, before the Royal Society of Medicine, Electrotherapeutic Section, London. Later, before the American Röntgen Ray Society, in 1912, also in 1913, I gave further papers on incompetency of the ileocolic valve. In 1912, I reported that out of a series of two hundred consecutive gastro-intestinal cases, one-sixth showed incompetency of the ileocolic valve as determined by the barium clysma. In August, 1913, I reported more than two hundred and fifty cases of ileocolic valve incompetency in a much more extensive series (fifteen hundred), in each of which the competency of the ileocolic valve was tested. It should be noted that since these were gastro-intestinal cases referred for bismuth-meal examination, in-

Fig. 5. Marked gas distention of the abdomen, which is evidently in the small intestine, the colon being filled by the bismuth enema. This reticulated appearance of the abdominal shadow is characteristic of gas distention of the small intestine, and is nearly always associated with ileocæcal valve incompetency.

Fig. 7. Röntgenogram of the colon after bismuth injection. Ileum filled at (*a*) by reflux through the ileocæcal valve. Note the dilatation of the entire right half of the colon, associated with spasticity of the iliac and pelvic colon (*b*), so often associated with ileocæcal valve incompetency.

cluding suspected gastric ulcer, gastric carcinoma, duodenal lesions, gall-bladder disease, chronic appendiceal disease, adhesions, kinks, torsions, spasms, and tumors of the colon, the presence of the ileocolic valve incompetency in this relatively large proportion of cases is not surprising. The majority of the patients were constipated.

Physiologists and anatomists agree that the normal ileocæcal valve action successfully closes the ileum against the return of colonic contents, both gas and fluid. The proof of the existence of antiperistalsis, especially the proof that it occurs in man, increases the probability that the ileocolic valve should be competent under normal conditions. Our observations in connection with surgical work, as well as the observations of other surgeons during various abdominal operations, give abundant confirmation of the belief that the normal ileocæcal valve is thoroughly competent. The ileocæcal valve of the dog and of the pig are competent, withstanding enormous gas and fluid distention of the colon. Numerous experiments have been performed to determine the normal competency or incompetency of the human ileocæcal valve. The consensus of opinion is overwhelmingly in favor of its normal competency.

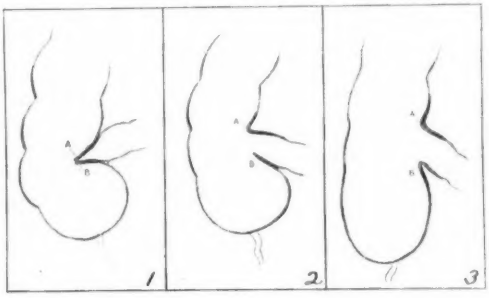


Fig. 6. Three figures (after Kellogg) illustrating ileocæcal valve incompetency: 1, normal ileocæcal valve; 2, incompetency of the valve associated with disinvagination of the upper lip; 3, incompetency of the ileocæcal valve with disinvagination of both lips.

Fig. 8. Röntgenogram after colon injection. Marked ileocæcal valve incompetency, associated with spasticity of the descending, iliac, and pelvic colon. Several small diverticula of the pelvic colon.

Fig. 9. Röntgenogram after the colon injection showing the small intestine widely filled through the incompetent ileocæcal valve. If one may judge the grade of incompetency by the degree of filling, and the degree of ileal stasis, the incompetency is very marked. Clinically the case was one of extreme alimentary toxæmia.

In fifty or more individuals I have repeated the test of the competency of the valve on more than one occasion to determine whether or not the competency observed was transient or permanent. On some occasions the patients have been examined a third, and even a fourth time, the interval between the different examinations being, in several instances, as long as three months. Without exception, when the ileocolic valve has been found incompetent to the enema on one occasion, it has been found incompetent at all subsequent observations.

Ileocæcal valve incompetency has been observed, not only after the clysma, but also (and this must have still greater significance) after the ingestion of the meal. In more than fifty cases I have definitely proved the regurgitation of ingested bismuth from the colon back into the small intestine. For instance, I have in numerous cases noted that the small intestine has been empty at the twelfth hour, all the bismuth-mixed content having passed on into the colon; yet observation the next morning has shown bismuth back in the terminal ileum, no new bismuth meal having been taken in the interim. This observation has been made repeatedly. If one doubts that the fact of incompetency is proved by the regurgitation of a bismuth enema into the ileum, he must certainly admit that the ileocæcal valve should normally prevent the regurgitation of ingested food back into the ileum, especially ingested bismuth.

A further evidence of the fact of ileocæcal valve incompetency is afforded by operative findings. In every instance where the ileocæcal valve proved to be incompetent to the enema, at operation the surgeon noted gas or fluid distention of the terminal ileum, which was often present to a distressing degree in spite of thorough efforts at pre-operative bowel cleansing. It is an easy matter to test the competency of the valve at the time of operation by the following method: The ileum being clamped off by the fingers of an assistant or by carefully protected instruments some twelve or fifteen inches from the

Fig. 10. Ileocæcal valve incompetency. Röntgenogram of the ileocæcal region following the evacuation of the bismuth enema. The ileum widely filled. A few traces remain in the cæcum and ascending colon. The appendix was adherent to the terminal ileum. Removal of the appendix, shown in Fig. 11, cured the incompetency.

Fig. 11. Retrocæcal appendix, adherent to the ileum, associated with ileocæcal valve incompetency. The removal of the appendix restored the competency of the valve.

ileocæcal valve, its contents are "milked" down through the ileocæcal valve into the cæcum. The normal ileocæcal valve prevents any regurgitation of the cæcal gas or fluid contents back into the ileum, even under considerable pressure, but the incompetent valve allows gas or fluid to pass back with readiness varying with the degree of incompetency.

Where the ileocæcal valve has proved competent to the enema, the surgeon has, in the great majority of cases, confirmed this observation by the test described. There are occasional exceptions, however, in which the valve proved incompetent at the time of the operation in spite of the apparent normal competency to the barium enema. I think the failure to detect these cases by röntgenologic examination may be due to certain sources of error which are apparently unavoidable. These sources of error and the details of technique, were discussed in a paper before the American Röntgen Ray Society.[1]

[1] Further Studies on the Ileocæcal Valve and Appendix, read before the American Röntgen Ray Society, Annual Meeting, Boston, October, 1913.

Still further proof of the normal competency of the ileocæcal valve is presented in the fact that the incompetency thus shown at operation has been cured in a number of cases by a simple surgical procedure. This ingenious operation for restoring the competency of the ileocæcal valve has been described by Kellogg in a recent paper.[2] The operation consists of skilfully placing several sutures in such a manner as to restore the invagination of the ileum without unduly narrowing its lumen. The operation is practically bloodless; it does not involve opening of the peritoneum, and it is quickly accomplished. At first Kellogg did not operate directly for the relief of the ileocæcal valve incompetency. The operation was devised and performed in those cases which had come to operation for the relief of marked ileal stasis, supposedly due to ileal kinks, and yet where, at operation, no ileal kink was found. Kellogg has since then felt that the field of this operation was somewhat more extensive, and he has performed it up to the present writing (January 15, 1914) in an even hundred cases. The majority of these ileocæ-

[2] Surgery of the Ileocæcal Valve, Surg., Gynec. & Obst., 1913, xvii, 563.

Fig. 12. Röntgenogram twenty-five hours post-cibum. The patient has had an ileosigmoidostomy. The transverse colon still retained a considerable residue on the third day. Retrograde filling of the colon has been the invariable finding in more than forty cases examined by the writer after ileosigmoidostomy.

cal valve repairs have been done in the course of operations for other causes, where the routine preliminary X-ray examination has shown ileal stasis to exist and where it appeared that the ileocæcal valve incompetency was the cause of the stasis.

The most convincing argument of the efficacy of this ileocæcal valve repair, and therefore of the important part ileocæcal valve incompetency plays as a factor in the production of ileal stasis, is found in the observation that whereas in all of these operated cases ileal stasis existed before operation, post-operative studies have shown that in every instance the emptying time of the terminal ileum has been markedly diminished and in the majority of the cases it has been reduced to seven or eight hours. Not only has there been röntgenological proof of lessened ileal stasis, usually lessened to within the normal limits, but there has been great improvement in the other clinical evidences of ileal stasis.

SUMMARY

While ileal stasis has been definitely shown to exist in connection with marked obstructing adhesions or kinkings of the terminal ileum, and while it is likely that spasm of the ileocæcal sphincteric mechanism may be another factor in the production of ileal stasis, it seems demonstrated that incompetency of the ileocolic valve offers a further and more tangible explanation of ileal stasis and that it is probably the essential causative factor in the majority of cases of stasis in the terminal ileum. Ileocæcal valve incompetency is almost invariably associated with the clinical evidences of intestinal stasis. Not all these patients have, as yet, a well-developed alimentary toxæmia. One writer has stated that, indeed, almost our only treatment, surgical or medical, is the "very primitive plan of keeping the bowels well cleared out." Short-circuiting and colectomizing operations are hazardous and often fail to cure. Appendicostomy has been performed by some surgeons. My experience in the röntgen study of these cases of intestinal stasis, both before and after operation, leads me to distinctly oppose the tendency toward operative interference for the relief of intestinal stasis. While we should not, for one moment, lose sight of what has been accomplished by surgical interference, yet according to Kellogg not more than one per cent of cases of intestinal stases are so severe that the operation of colectomizing or short-circuiting is justifiable. As Keith has stated, the colon is more of a misused than a useless structure, owing to the extraordinary changes which have taken place in the diet of man in civilized countries. Surgery should not be seriously considered as the cure for ileal stasis until a most thoroughgoing trial has been made of the various dietetic and mechanical measures at our command. If an operative measure seems advisable, recognition of ileocolic valve incompetence as a potent cause of ileal stasis may present a course of surgical treatment free not only from the dangers associated with short-circuiting with or without colectomy, but actually calculated to restore normal physiological function.

DIAGNOSIS OF THE PARTICULAR FORM OF HYDRONEPHROSIS DUE TO MOVABLE KIDNEY

By HOWARD A. KELLY, M. D., and ROBERT M. LEWIS, M. D., Baltimore

NOTHING looks more marvelous to the uninitiated and nothing is more gratifying to the expert than good diagnostic work in diseases of the kidney.

I well remember sitting on the benches at the University of Pennsylvania in the late seventies, when William Pepper, Professor of Medicine, brought before the class "a rare case of a movable kidney. . . . Not many, perhaps seven, had been reported in the living, and in any individual case it required great diagnostic skill to determine that the organ felt was a kidney." This simply shows that while thermometers, stethoscopes, and direct auscultation and percussion were much in vogue a generation ago, how little our forefathers used their hands in examining their patients. Nowadays one good clinic can often equal the thenadays world's record in one active morning.

One of the diseases that has crept out of obscurity into the light of day is hydronephrosis. Formerly we only distinguished the end-product, a great tense sac of fluid in a shell of a kidney. Now we recognize all the stages from the incipiency in moderate distention up to the big, cystic, practically dead kidney. The advantage of the change lies in the fact that in its early stages the condition is curable without mutilation, while in the latter it is not. It is of a case of this group that I desire to speak particularly, as I hope to demonstrate that, by a combination of catheterization of the kidney and an X-ray examination with reasoning on known facts, not only can a diagnosis of hydronephrosis be made, but the exact form can be determined before operating.

The case was that of a patient of Dr. D., 33 years old, married, and the mother of one child 15 months old. The history given was somewhat vague, but the patient believed herself to be suffering from some form of gastro-intestinal disturbance. For years she was troubled with attacks of pain in the right upper abdomen. This pain as a rule radiated to the right scapular region and at times seemed to be general throughout the abdomen. At the time of examination a painful point was noted midway between the region of the right kidney and the gall-bladder. This passed downward to the crest of the ilium and down the outer side of the right leg.

The fact that the character or quantity of food taken appeared to make no difference in the symptoms would appear to argue against a gastric origin of pain.

The symptoms were not sufficiently acute or definite to indicate the presence of gall-stones; for this, too, the pain did not seem to have been sufficiently severe. There has been and is no tenderness in the region of the gall-bladder; there has never been any jaundice.

Appendicitis was excluded in the right iliac fossa, and the pain area appeared to be too high to make this diagnosis likely. The bowels were obstinately constipated, but not particularly so at the time of the attacks.

Careful physical examination failed to exactly localize the pain or to discover any definite regions of tenderness. However, a most important find was made; to wit, the right kidney was catheterized with a wax-tipped catheter which showed no scratch-marks on withdrawal.

One and one-half hours after hypodermatic insertion of 1 ccm. of phenolphthalein, 1 ccm. of urine was secreted by the right kidney which showed only a minute trace of the injected substance. In the same time 35 ccm. of urine was put out by the left kidney with a phenolphthalein content of 18.2. Eighty cubic centimeters of sterile boric acid colored with methylene blue was injected in the right renal pelvis through the renal catheter while a glass catheter was in the bladder to show any reflux. This produced a mild pain in the right iliac fossa, near the iliac crest, which the patient at once identified as the charac-

Fig. 1. The excellent radiogram shows the great distension of the renal pelvis filled with the silver iodide emulsion. In the reproduction there is a distinct break between the shadow of the injected ureter and the bottom of the pelvis. The original radiogram shows a fine dark line connecting the two indicating the almost obliterated lumen between them.

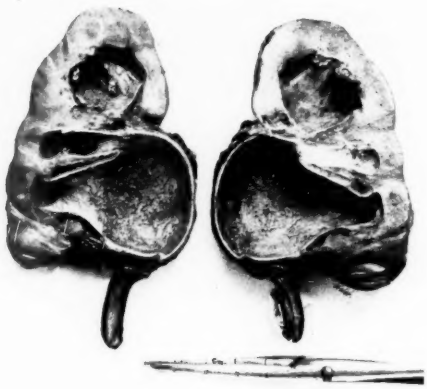


Fig. 2 shows the divided kidney after its removal. Notice the great distention of the pelvis with the kinking, adherent ureter on its under surface.

teristic pain from which she suffered. Let me emphasize the fact that only a small part of the solution injected returned through the catheter; in other words, the remainder was trapped in the renal pelvis.

The ureteral catheter was again introduced the following day and passed up to a point a few centimeters below the renal pelvis. About 10 ccm. of a five-per-cent emulsion of silver iodide and 50 ccm. of a one-per-cent mixture of the same substance were then slowly injected into the renal pelvis. A radiogram was then taken, after which some solution escaped by the catheter and a part was washed out. There was but little pain as the result of the injection.

We have here a reproduction of the splendid skiagram which, coupled with the history and the physical examination, made possible a most accurate diagnosis of the cause and seat of the trouble.

The ureter is distended with the silver iodide emulsion from the tip of the catheter up to a point one centimeter below the renal pelvis. The large dilated pelvis lies beautifully outlined above. Between pelvis and injected ureter is an area in which the silver iodide has not manifestly lodged. This evidently represents the site of the obstruction which is due, not to the presence of a stone, but to a kinking of the ureter just below the renal pelvis.

A diagnosis of chronic intermittent hydronephrosis was made and the right kidney removed.

At operation the kidney was found enlarged to a mere shell. The enlarged pelvis was readily exposed, and as, expected, a right-angle kink was found in the ureter just where it left the renal pelvis. The ureter itself was fast adherent to the lower surface of the pelvis for a distance of one and one-half centimeters. It then bent sharply downward in its normal direction.

The ureteral lumen was opened just below the kidney, but none of the contents of the renal pelvis escaped until the dense adhesions doubling the ureter on to the pelvis were dissected free. A gush of watery fluid containing particles of silver iodide then followed, and in this way the mechanism of the obstructing valve was clearly demonstrated. The arrangement of the parts was like that of the structures at the internal inguinal ring designed to prevent hernia. Here, unfortunately, the valve proved itself all too

competent and ended by bringing about the destruction of the kidney.

Section of the kidney shows but a rim of cortex. The hydronephrotic sac contained a considerable amount of the injected silver iodide emulsion. This is contrary to the experience that we have had in the case of injection of the pelves and ureters of actively functionating kidneys where all traces of the iodide are generally removed within forty-eight hours. In such a case, unless nephrectomy is to follow immediately, the injection of any foreign material into the renal pelvis is undesirable if not actually dangerous.

Let us now reason a little about this most interesting patient.

In the first place, every pain which is persistently lodged in one side, in a patient who is not highly neurotic or hysterical, usually arises from some definite trouble in some one organ. When the pain is intermittent and more or less diffuse, extending at times down over the outer aspect of the thigh, it is usually renal in origin.

The injection of 80 ccm. through the renal catheter, which failed to return, was highly suggestive of a valvelike orifice of the ureter and, therefore, of hydronephrosis of that grade.

The bringing on of an attack similar to those complained of settled the diagnosis of hydronephrosis. The X-ray of the renal pelvis distended with silver iodide solution, five per cent, now comes in with exquisite confirmation of the diagnosis, and with additional important information. In the first place, the ureter ends abruptly at the renal pelvis. The pelvis is large and distended with the silver solution. Between the two, parallel to the pelvis, a close examination can distinguish a fine line like a tiny thread of injection. These findings can always be interpreted as demonstrating, as clearly as an autopsy, that we are dealing with a hydronephrotic kidney, with a valvelike ureteral orifice, which is bound down flat and compressed against the renal pelvis for about one and one-half centimeters at its upper end. This was precisely what was found at the operation.

REGENERATION OF CARTILAGE AND BONE WITH A SPECIAL STUDY OF THESE PROCESSES AS THEY OCCUR AT THE CHONDROCOSTAL JUNCTION

By S. L. HAAS, M. D., San Francisco
From the Pathological Laboratory of Stanford University Medical School

THE two tissues, cartilage and bone, when fully developed are very easily distinguished from one another, and there is nothing to suggest that they have a close developmental relationship. Cartilage is flexible, cuts easily, and has a smooth, glistening surface and a homogeneous structure. Microscopically, the cells which are situated in a uniform ground substance are of a single type varying only in size — from large and round at the center to small and flat toward the periphery, where they gradually pass into a surrounding membrane called the perichondrium. Bone is firm, cuts with difficulty, and has a rough, irregular surface with a complex architecture. Microscopically, the cells are of various types, which in the center form the complex marrow, beyond which is the cortex, made up of characteristic bone-cells lying in a uniform ground substance. The entire structure is surrounded by a thin membrane called the periosteum. In studying the embryological origin of cartilaginous bone, its close relationship to cartilage becomes apparent, as it will be found to have arisen from a blastemal syncytium of white fibrous tissue and to have passed through an intermediate cartilaginous stage.

This transition from the fibrous connective tissue to the simple cartilage and the complex bone involves as intricate a developmental problem as is met with in any of the developmental changes within the body. Here, as in all other developmental and regenerative changes, there is some unknown factor or force that initiates these transformations. This influence is often referred to as the inherent organization of the germ; but we have no definite conception as to what that organization is. In the study of cartilage and bone it will be noticed that certain cells possess this inherent tendency to produce these specific types of tissue; and although we cannot hope to determine what the stimulating factor may be, we should at least be able to arrive at a uniform interpretation of the various steps of the process.

A review of the histogenesis of cartilage reveals the fact that there are still a number of disputed points in regard to the formation and structure of this simple tissue. It is not within the scope of this paper to deal with the minute cellular changes that take place in the regenerating cartilage, but there are certain fundamental points that must be described. A recent article by K. von Korff (1) gives a detailed description of the development of normal cartilage which well exemplifies the complexity of the process. In the present discussion the chief problems to be considered are the relative importance of the original cartilage and of the perichondrium in forming the new cartilage.

A review of the histogenesis of bone likewise reveals the fact that there are a number of disputed points regarding the method of its formation. It is not necessary to deal here with the minute cytological changes that take place in the regenerating bone, since in this discussion the chief problems to be considered are the relative importance of the original bone and of the periosteum in forming the new bone.

In the transformation of cartilage into bone the perichondrium takes a very active part in the perichondrial and in the endochondrial ossification. Following the penetration of the perichondrial buds into the cartilage, changes take place by which the marrow cavity and the cancellous bone are formed. The exact manner in which the cartilage is changed into bone has not been fully ascertained, some investigators believing that there is a direct change of cartilage-cells into bone-cells, while others, the majoirty, believe that the new bone is formed outside of the old cartilage, which only acts as a directing framework for the new bone. Coincident with the changes

that take place within the center of the cartilage there is a direct deposition of bone beneath the perichondrium. After the bony stage has been reached the perichondrium becomes the periosteum and the chondroblast becomes the osteoblast. Thus it is evident that there is a very close relationship between the perichondrium and the periosteum, between the chondroblast and the osteoblast, and between cartilage and bone; and it would be only natural to expect a certain parallelism in the method of regeneration of two tissues so closely related in their development.

It is to be hoped that the following experiments will aid in explaining some of the problems concerning the method of regeneration and development of bone and cartilage.

All of the observations in these 57 experiments were made upon the ribs and costal cartilages of rabbits; therefore the deductions as regards the regeneration of cartilage are naturally limited to hyaline cartilage, and, as regards the regeneration of bone, are limited to the bones that arise from cartilage.

The various subjects will be taken up in the following order:

I. Regeneration of cartilage.
II. Regeneration of bone.
III. Regeneration of bone and cartilage at the chondrocostal junction.
(*a*) Regeneration of bone at the junction.
(*b*) Regeneration of cartilage at the junction.
(*c*) Regeneration of bone and cartilage at the junction.

I. REGENERATION OF CARTILAGE

There is a rather general idea that cartilage possesses only a slight power of regeneration, and it is even held by some that this power is entirely lacking. The greater number of investigators admit that cartilage has the property of regenerating, but there is no uniformity of opinion as to the exact method.

M. Matsuoka (2) gives a complete and concise review of the principal articles that have appeared under regeneration of cartilage up to the year 1904. The consensus of opinion at that time was that the regeneration takes place only from the perichondrium, but there was a difference of opinion as to the exact method by which the perichondrium produced the new cartilage. It was believed by some that the perichondrium only changed the surrounding connective tissue into cartilage, while others believed there was a direct proliferation of the perichondrial cells. A few investigators thought that the regenerated cartilage came from the old cartilage, or from the old cartilage and the perichondrium together. Matsuoka concluded from his experiments on the ear cartilages of rabbits that the perichondrium was the only source for the new cartilage.

Since the appearance of Matsuoka's article a few important papers have appeared, and they will be shortly reviewed.

An article by Maltesta (3) contains some interesting points. His experiments were performed upon rabbits at the age of eight to ten months. He either scratched the perichondrium from the rib cartilage, cut the cartilage in two, or removed a triangular piece of cartilage. He reported that there was a calcification of the cartilages that were operated upon in all of the animals. A distinction is made between the first to the seventh and the eighth to the twelfth ribs. In the first to the seventh, which are designated as the thick ribs, after a complete incision there was a perichondrial growth on the outside, then a calcified layer, and in the center a layer of cartilage. In the eighth to the twelfth ribs, designated as the thin ribs, the central layer was also calcified. Only in small incomplete cut wounds or in incompletely calcified cartilage can a partial healing through cartilage tissue take place. Exceptionally, the cartilage and connective tissue surrounding the wound produces young connective tissue, which later on may be changed into hyaline cartilage. The change of the connective tissue always takes place under the influence of the perichondrium. The cartilage-producing properties of the perichondrium are greatest in minor injuries and might be entirely lacking in the larger destruction of cartilage. Although he acknowledges the importance of the perichondrium, he does not make clear whether it directly forms cartilage or whether it only influences the new-formed connective tissue to form cartilage.

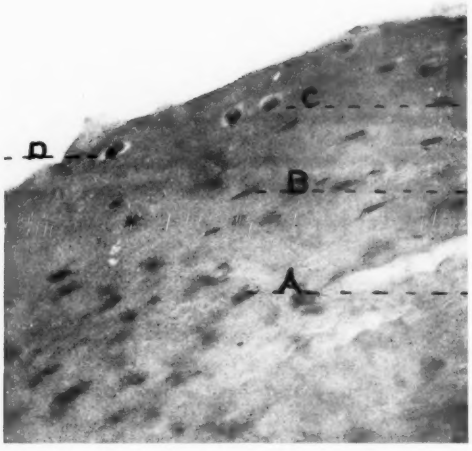


Fig. 1. Normal stripped-off perichondrium. A, fibrous outer layer; B, layer of platelike nuclei; C, oval nuclei; D, paired vesicular nuclei. (Microphotograph, Obj. 1/6; Occ. 1 inch, B. & L.)

The study of transplanted pieces of cartilage gives us some information as to the part the different regions of cartilage take in the regeneration.

Axhausen (4), from his experiments, concluded that only the part near the perichondrium formed new cartilage.

Davis (5), in a series of experiments on the transplantation of the rib cartilage of dogs from three months to two years of age, found no evidence of degeneration, either macroscopically or microscopically, after the lapse of four months. The perichondrium was also transplanted in these experiments.

Before proceeding with the experimental part of this work it will be necessary to give a definition of the perichondrium as it is here considered. Since the experiments were made upon the ribs the conclusions are necessarily limited to hyaline cartilage with perichondrium, although they will probably apply to other kinds of cartilage.

The perichondrium of the costal cartilages is a thin membrane which can be separated from the underlying cartilage providing the exact line of cleavage is found. At the chondrocostal junction it becomes thicker and more adherent and is continuous with the periosteum.

Under the microscope it is impossible to make out any separation between the perichondrium and the true cartilage. The outer layer of the perichondrium consists of loosely arranged fibrous tissue beneath which are longitudinally placed platelike nuclei. In the next layer the nuclei are larger, oval in shape, and stain lighter, and they are not so close together. These latter nuclei shade off gradually into a group which are slightly larger and have a more vesicular appearance. Many of the latter are in pairs as though they were dividing. As will be seen from the description of the stripped-off perichondrium, this layer marks the line of separation between the perichondrium and the cartilage. The next cells are the very youngest of the cartilage cells, which are often removed with the perichondrium.

To determine accurately the constituent elements of the perichondrium, it seems better to describe its appearance as we find it after it has been stripped from the cartilage. Under high magnification the perichondrium is seen to consist of an outer, loosely arranged fibrous layer, a median compact layer with platelike nuclei, and an inner layer of oval nuclei, among which are paired vesicular nuclei (Fig. 1). Scattered throughout the inner layers there are some cells which are either young or intermediate cartilage-cells.

The examination of the cartilage after the removal of the perichondrium shows on the surface a varying appearance on account of the irregular separation of the perichondrium. In places the young cartilage-cells are on the outer margins, while at other points the paired vesicular nuclei are noticed.

From this detailed description it is seen that there is no sharp separation between the perichondrium and the underlying cartilage. It is given in order that the author's conception of the structure of the perichondrium may be fully understood and the following experiments correctly interpreted.

SUBPERICHONDRIAL RESECTION OF CARTILAGE

Method. All of the experiments were performed under ether anæsthesia. An incision

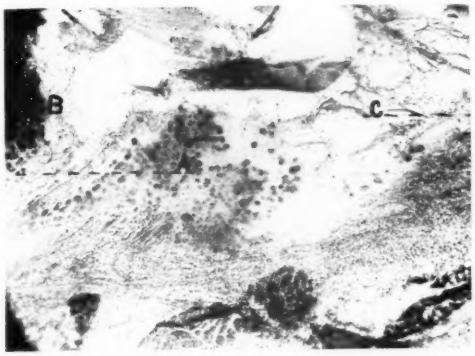


Fig. 2. Regeneration of cartilage from the perichondrium five days after a subperichondrial resection. A, regenerated cartilage from the perichondrium showing multinucleated cells; B, cartilage-stump at one end; C, perichondrial gutter containing fibrin. (Microphotograph, Obj. $\frac{2}{3}$; Occ. 2 inch, B. & L.)

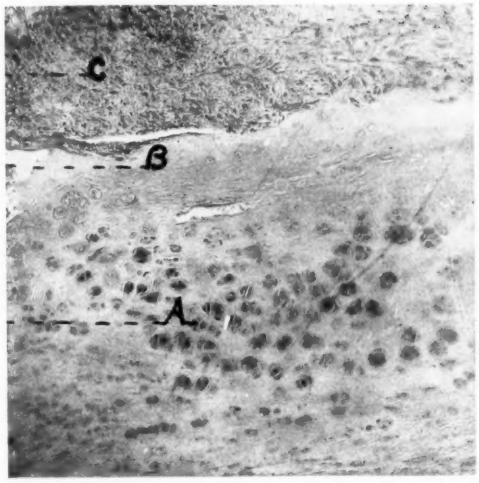


Fig. 3. Regeneration of cartilage from perichondrium seven days after resection. A, regeneration of cartilage from the perichondrium; B, degeneration of cartilage that was attached to the perichondrium; C, perichondrial gutter. (Microphotograph, Obj. $\frac{2}{3}$; Occ. 1 inch, B. & L.)

was made through the skin and muscle down to the cartilage of the ribs. One of the larger cartilages was selected, and a longitudinal cut was made through the perichondrium. By careful dissection the perichondrium was separated from the underlying cartilage, but owing to the shape and flexibility of the cartilage it was difficult to remove it completely. A piece of cartilage from one to two centimeters in length was removed, after which the severed tissues were approximated with silk sutures. A bandage was applied to the chest and the animal allowed its freedom.

Results. In 11 out of 13 experiments of this nature, cartilage was found in increasing amounts proportional to the length of time that had elapsed — which was 5, 10, 15, 20, 23, 30, 36, 38, and 46 days, respectively. In two cases of 15 and 20 days' duration, no evidence of new cartilage was found on macroscopical examination.

In order to determine the method of regeneration, a series of sections were made at 5, 7, 10, 15, and 20 days. The tissue was fixed in Orth's fluid, embedded in paraffin and stained with hæmotoxylin and eosin or van Gieson.

Experiment 1; Rabbit 267; 5 days.

Gross examination. The perichondrial gutter is filled with blood-clot.

Microscopical examination. The stump of the cartilage shows some slight proliferating changes on the surface near the perichondrium. Back from the cut edge a proliferation in the region of the perichondrium is to be found. The perichondrial gutter is filled with fibrin and young connective tissue. The perichondrium cannot be identified at this time. The nuclei of the inner layer at various places have lost their staining power, although the rest of the cells appear to be proliferating. In several parts of the section there are collections of groups of nuclei which have the appearance of undergoing active division (Fig. 2).

Experiment 2; Rabbit 7^2; 7 days.

Gross examination. The perichondrial gutter is filled with new tissue the exact nature of which cannot be determined.

Microscopical examination. The cartilage stumps end abruptly, and there is no evidence of proliferation except along the outer margin near the perichondrium. There is some proliferation of the perichondrium extending back of the cartilage stumps. The perichondrial gutter is filled with young connective tissue formed by the organization of the exudate as previously described. The perichondrium shows changes throughout its entire structure. In the innermost layers the nuclei have lost their staining reactions (Fig. 3). This degenerating tissue looks like cartilage-cells that have been removed with the perichondrium; and it seems to indicate that even if cartilage is removed with the perichondrium. it takes no part in the regeneration. The remainder of the perichondrium is actively proliferating to form new cartilage tissue.

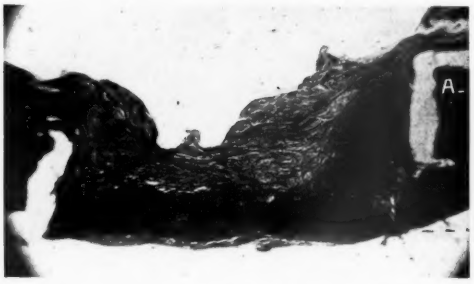


Fig. 4. Regeneration of cartilage fifteen days after subperichondrial resection. A, cartilage-stumps; B, new cartilage from the perichondrium. (Microphotograph, Obj. 2 inch; Occ. 2 inch, B. & L.)

Experiment 3; Rabbit 426; 10 days.

Gross examination. There is a tubular mass of tissue in the perichondrial gutter, but its exact identity cannot be determined.

Microscopical examination. At this stage there is a marked growth of new cartilage, the greater part of which comes from the perichondrium. There is a considerable amount of new cartilage about the cartilage stumps, and in places it is in such close contact with the original cartilage that it appears to have originated from it. In other places there is a direct transition from the new-formed cartilage to the surrounding young connective tissue, and from such a picture the interpretation might be made that this cartilage has been formed by a metaplasia of connective tissue.

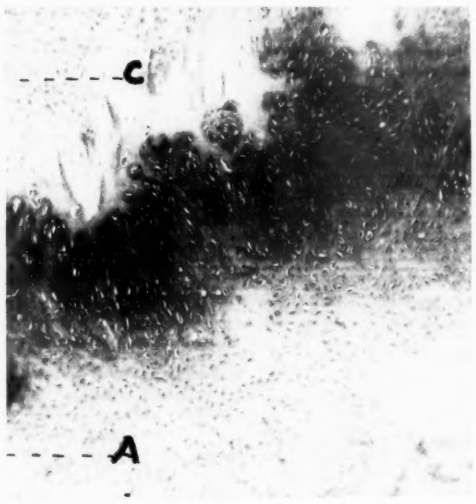


Fig. 5. Regeneration of cartilage from the perichondrium fifteen days after subperichondrial resection. Higher magnification from section in same series as Fig. 4. A, outer layer of perichondrium; B, new cartilage from perichondrium; C, connective tissue in perichondrial gutter. Notice the change in advance of the new cartilage. (Microphotograph, Obj. 3/5; Occ. 1 inch, B. & L.)

Fig. 6. Condition fifteen days after removal of cartilage with its perichondrium. A, cartilage-stumps; B, connective tissue between stumps showing entire lack of regeneration of cartilage. (Microphotograph, Obj. 2 inch; Occ. 2 inch, B. & L.)

Experiment 4; Rabbit 321; 15 days.

Gross examination. There is almost complete filling of the gap with new cartilage.

Microscopical examination. The cartilage stumps end abruptly. The greater part of the regenerated cartilage arises from the perichondrium (Fig. 4). All the layers of the perichondrium appear to be taking part in this new formation of cartilage; and the connective tissue in advance of the new car-

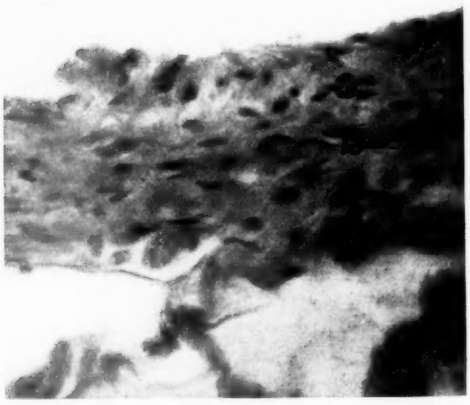


Fig. 7. Normal stripped-off periosteum. A, outer fibrous and fibro-elastic layer; B, layer of platelike nuclei; C, layer containing round and oval nuclei. (Microphotograph, Obj. 1/6; Occ. 1 inch, B. & L.)

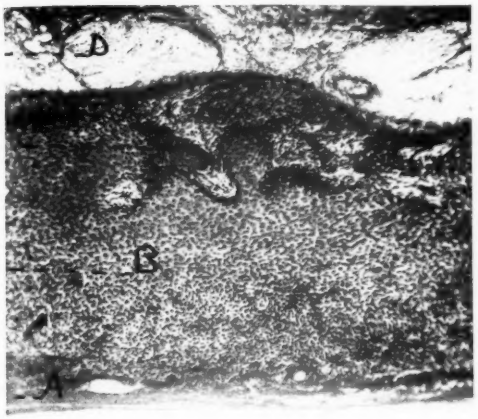


Fig. 8. Regeneration from the periosteum five days after a subperiosteal resection. A, outer side of periosteum; B, new-formed chondroid tissue from the periosteum; C, osteoblasts capping the new tissue; D, organized fibrin in the periosteal gutter. (Microphotograph, Obj. 2/3; Occ. 2 inch, B. & L.)

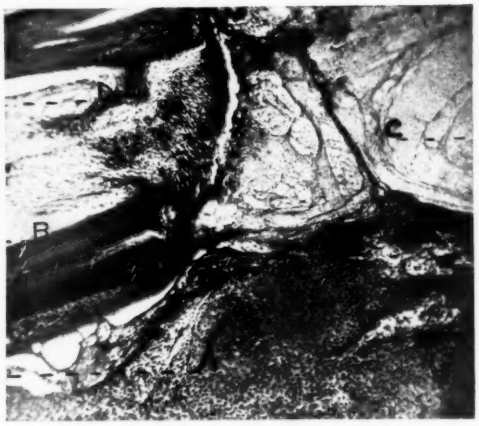


Fig. 9. Same as Fig. 8, only near the cut end of the rib. A, periosteal new-formed chondroid tissue; B, lower layer of cortex; C, perichondrial gutter; D, slight growth from endosteum; E, upper layer of cortex. (Microphotograph, Obj. 2/3; Occ. 2 inch, B. & L.)

tilage, which is formed independently of the perichondrium, is also assuming a cartilaginous structure (Fig. 5). This again suggests that the perichondrium is exerting some influence over the connective tissue to transform it into cartilage, and it is possible that it is a source of some of the cartilage. A short distance away from the stumps there is some new cartilage which is connected neither with the perichondrium nor with the original cartilage, and its exact origin cannot be definitely determined from these sections.

Experiment 5; Rabbit 271; 20 days.

Gross examination. The entire perichondrial gutter appears to be filled with new cartilage.

Microscopical examination. At this stage the cartilage formation is much denser. The independence of the perichondrial origin of that from the stumps is quite apparent. The cartilage stumps appear to be degenerating in the cut surface, and within this area there is a suggestion of calcification of the old cartilage.

Conclusions. From the foregoing experiments it is obvious that the chief source of the regeneration of cartilage is from the perichondrium. The change is produced by a proliferation of certain cells of the perichondrium to form the young cartilage-tissue.

In case any of the true cartilage is removed with the perichondrium, it does not take part in the regeneration, but undergoes degeneration.

From some of the sections it would seem that there is a direct transformation of connective tissue into cartilage, due perhaps to some specific stimulus of the perichondrium or of the cartilage.

The cartilage stumps take a very inactive part in the regeneration, and at times undergo degenerative changes. It is possible that the cartilage might have some tendency to transform the surrounding connective tissue into cartilage.

Some investigators have described calcareous changes in the regenerated cartilage after the thirty-fifth day, in animals that were from eight to ten months of age. In these experiments there was never any evidence of calcification of the regenerated cartilage even after the lapse of forty-six days.

Various observers have failed to find regeneration when a considerable piece of cartilage had been removed; but in the above experiments regeneration occurred regardless of the amount of cartilage removed.

RESECTION OF A PIECE OF CARTILAGE WITH ITS PERICHONDRIUM

In order to emphasize the importance of the perichondrium as a factor in the regeneration of cartilage the following additional experiments were performed.

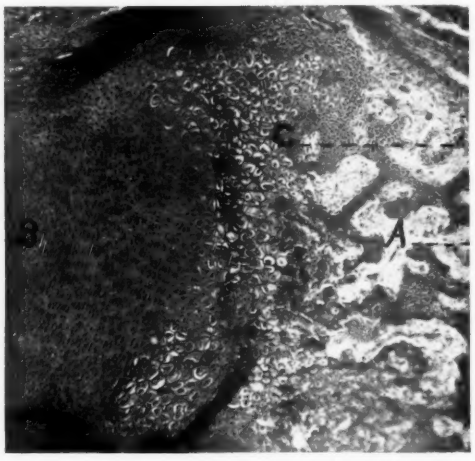


Fig. 10. Regeneration of bone and cartilage twenty days after a subperichondrial and subperiosteal resection of the chondrocostal junction, with restoration of the junction A, regeneration on the osseous side of the junction; B, regeneration on the cartilaginous side; C, restoration of chondrocostal junction. (Microphotograph, Obj. 3/5; Occ. 2 inch, B. & L.)

Method. This set of experiments differed from those just described in that the perichondrium was removed with the resected piece of cartilage. After such a resection if any regeneration occurs it must originate from the perichondrial-covered stumps at either end of the gap.

Results. In three experiments of this nature gross examination showed entire absence of cartilage formation between the two stumps after the lapse of 15, 23, and 35 days, respectively. In the experiment which lasted 15 days microscopic examination verified the findings.

Experiment 6; Rabbit 321; 15 days. This experiment is to be compared with Experiment 4, as it was carried out on the same animal, at the same time, and under similar conditions. It differs from the other because in this case the perichondrium was removed with the cartilage.

Gross examination. There is no evidence of growth from the cartilage stumps or the intervening tissue.

Microscopical examination. There is a slight regeneration of new cartilage near each of the cartilage stumps which appears to come from the perichondrium. The gap between the two stumps is filled with connective tissue and there is an entire absence of new cartilage (Fig. 6). In Experiment 4, which differs only in that the perichondrium was allowed to remain, there is a considerable amount of new cartilage in the gap between the two stumps (compare Figs. 4 and 6).

Conclusion. No doubt can remain as to the important part the perichondrium takes in the regeneration of cartilage; also that connective tissue, without the aid of perichondrium or cartilage, is not capable of changing into cartilage.

II. REGENERATION OF BONE

In a previous paper (6) concerning the relation of the periosteum to the regeneration of bone, I came to the conclusion that the periosteum had the power to regenerate bone independently of any preëxisting bone, especially in the presence of blod clot.

In that article a general review of the literature was given, so it will only be necessary here to call attention to the important articles that have appeared since that time.

Ryerson (7) reports, from the röntgenoscopic examination of the early changes that take place in fractures, that there is no regeneration from the periosteum, because he does not see any new bone formed in the angle where the periosteum is stripped up from the cortex. It is hardly to be expected that the very early changes in bone formation would be noticeable in a röntgenogram, especially where there is an absence of lime salts. However, if one makes a microscopical study of these early changes in fractures, it is easy to see that there is a new formation of bone at the place where the periosteum is elevated from the cortex.

Gallie and Robertson (8) give their findings in a series of experiments and conclude that the periosteum is unable to regenerate bone. In their experiments they have separated the periosteum from the cortical bone by means of tinfoil or other metallic substances, and they found no evidence of bone formation from the periosteum. By placing the periosteum in contact with a metal or foreign body they have not placed it under conditions which are favorable for proliferation. If in these experiments a layer of blood-clot had been inserted between the stripped-up peri-

osteum and the metal plate, it is possible that there would have been new bone formed from the periosteum owing to the presence of a more stimulating and nutrient pabulum.

McWilliams (9) concludes from his experiments on the transplantation of bone that the periosteum is of importance not so much for its osteogenic properties as for its power to increase the blood supply. The exact manner in which the periosteum increases the blood supply is not stated. It would seem that the periosteum would prevent the penetration of blood-vessels, thereby decreasing rather than increasing its vascularity.

Groves (10), in an excellent and extensive article on the experimental production and treatment of fractures, ascribes no osteogenetic function to the periosteum. One cannot but feel that he is somewhat influenced in his deductions, as a study of his experiments and photographs presents just as much evidence for the osteogenetic power as against it. Like Macewen, he defines the periosteum as consisting of a fibrous layer only; but in his experiments he makes use of the same membrane that all operators and investigators consider to be the periosteum, which consists of more than a fibrous layer as stated in his definition. As will be shown later, the membrane that is removed with care from the bone, which is considered by all as the periosteum, has a definite microscopical appearance. Naturally, the outer layer of this membrane is not osteogenic because if it were there would be just as much growth on the outside of the periosteum as within, but the immediate layer of cells beneath this layer is a definite part of the periosteum and is capable of producing bone. If this layer is not to be included in the periosteum, then there must be a new definition for periosteum by which an artificial separation of a definite anatomical structure is described.

A recent article by Mayer and Wehner (11) on the regeneration and transplantation of bone presents some very decisive evidence against the theory of Macewen and his followers. They found that young periosteum, when transplanted into muscle, was capable of regenerating bone. They also found that the periosteum, after subperiosteal resection of the ribs, was capable of regenerating new bone. In another set of experiments they placed a glass or steel cap beneath the periosteum, which extended into the cortex for a short distance so as to prevent periosteal ingrowth. There was failure of regeneration of bone inside the capsules when there was no penetration of the periosteum. This emphasizes the importance of the periosteum in all regenerative processes of bone and shows the relative inactivity of cortical bone. In their transplantation experiments they agree with Axhausen that the greater part of regeneration takes place from the periosteum, but that there is also proliferation from the endosteum.

On account of the confusion that has arisen over the definition of the periosteum it becomes imperative to give an exact description of that membrane.

The periosteum is usually described as consisting of an outer fibrous layer, a middle fibro-elastic layer, and an inner osteogenetic layer in which are a large number of embryonal connective-tissue cells (the osteoblasts). After growth has ceased this osteogenetic layer is reduced to an inconspicuous stratum. According to Macewen, there is a loose layer of areolar tissue beneath the periosteum.

Examination of the periosteum covering the rib shows an outer loose fibrous and fibro-elastic layer. This latter layer merges into a group of cells with platelike nuclei which are closely packed together and which extend almost to the cortical bone. On approaching the cortex one can see some moderate sized oval vesicular nuclei. It is possible that these two kinds of cells are dormant osteoblasts. On the outer surface of the cortex the nuclei are spindle-shaped and pycnotic. In a normal section there is no demonstrable separation between the periosteum and the cortex excepting where artificially separated during the process of cutting.

Examination of the stripped periosteum shows an outer fibrous and fibro-elastic layer which merges into a cellular layer of the platelike nculei, as described above (Fig. 7). On the inner side of this fibro-elastic layer are groups of cells with vesicular oval nuclei, and others with pycnotic round nuclei, but there are never any cortical bone-cells to be found.

This description of the periosteum agrees with that usually given by the embryologists, anatomists, and histologists who in general believe that it has osteogenetic properties; and it has been so applied as a basis of the following experiments.

Examination of the surface of the bone after removal of the periosteum shows groups of cells with platelike and vesicular nuclei which are identical with those found on the inner portion of the periosteum, and it seems more probable that these are portions of adherent periosteum than that they are portions of the cortical bone.

SUBPERIOSTEAL RESECTION OF A RIB

Method. One of the larger ribs was selected, and after the periosteum had been carefully separated a piece of rib from one and one-half to two centimeters in length was removed. No attempt was made to check any slight bleeding into the periosteal gutter. The tissues and the skin were approximated with silk sutures.

Results. In all of the seven experiments of this nature there is regeneration of bone in various stages in the periosteal gutter. In the very early stages the new tissue is cartilaginous in nature, but at ten days the deposition of new bone is quite noticeable. A detailed description will be given only in those cases in which a microscopical examination was made; namely, at 5, 11, 15, 26, and 29 days, respectively.

Experiment 7; Rabbit 267; 5 days.

Gross examination. Nothing but blood can be seen in the periosteal gutter.

Microscopical examination. The periosteum cannot be recognized at this time, as there has been a proliferation of all the cellular elements within the outer fibrous layer. In the periosteal gutter there is a light bluish staining tissue which looks like young cartilage and which is capped by a layer of osteoblasts (Fig. 8). The cut ends of the ribs show absolutely no evidence of new growth. There is a slight amount of new bone formed from the endosteum (Fig. 9). A study of the angle formed by the stripped-up periosteum and the cortex shows even at this time a deposition of osteoid tissue.

The question arises as to the origin of this new bone at the angle. The possibilities are that it can come from the periosteum, from the cortical bone, or from the osteoblasts that have wandered out from the haversian canals and the marrow of the bone. If the osteoblasts came from the haversian canals and the marrow, it is surprising that there is no new osseous tissue at the cut ends, at which place there is ample opportunity for free migration of such cells. If the bone was formed from the cortex, then it should be uniformly deposited along the surface of the cortex and on the cut ends of the cortex; but the sections do not show that this takes place. Therefore, it must be that the new bone has originated from the periosteum, and there is considerable evidence that this is the case. It is noticed that there is a uniform transformation of the periosteum to chondroid tissue which is just as marked at the center of the gap as at the ends (compare Fig. 8 from the center with Fig. 9 at the end).

Experiment 8; Rabbit 275; 11 days.

Gross examination. The periosteal gutter is filled with new tissue which appears to be cartilaginous near the bone and calcareous toward the center.

Microscopical examination. The periosteal gutter is filled with new tissue which for the most part is of a cartilaginous nature, but in which there are scattered areas of osseous tissue. The periosteum is no longer recognizable, the greater number of its elements being involved in the formation of the new tissue. There is no regularity in the distribution of the osseous and cartilaginous tissue. The process is slightly more advanced than in the previous experiment.

Experiment 9; Rabbit 273; 15 days.

Gross examination. With the exception of a small amount of cartilaginous tissue near the stumps, the periosteal gutter is filled with osseous tissue.

Microscopical examination. One is immediately impressed with the large amount of bone present at this time, as it practically fills the entire space. Under the high power the remains of the cartilage cells can still be seen; and although it is generally denied that the cartilage cell can be transformed into a bone-cell, it often appears as though such a process were taking place in these regenerative changes. There is a considerable proliferation from the bone stumps, and this new bone is becoming intimately united to the periosteal bone. The periosteum is beginning to assume its normal appearance.

Experiment 10; Rabbit 994; 26 days.

Gross examination. There is complete filling up of the periosteal gutter with calcareous material, excepting for a small island of cartilage near the center.

Microscopical examination. The process differs from that found in Experiment 9 in that the osseous tissue is more dense.

Experiment 11; Rabbit 73; 29 days

Gross examination. There is complete filling of the periosteal gutter with new bone.

Microscopical examination. There is less bone and more cartilage at this time than in the previous experiment, in spite of the fact that a longer time had elapsed. There is no definite order in the arrangement of the cartilage and the bone.

Conclusions. From the microscopical study of these cases it is apparent that the periosteum is very actively concerned in the regeneration of bone. There is at first a proliferation of all its cellular elements to produce a cartilaginous material, which is in turn transformed into bone. In the very early stages there is no growth from the cortex or from the marrow, but later there is a limited amount of regeneration from these parts.

There is considerable irregularity in the relation of and the amount of bone and cartilage formed at different periods, which might be dependent upon the age of the animal, the amount of tissue to be regenerated, the presence or absence of blood-clot, and the injury to the periosteum.

From many of the sections it appears as though there is a direct transformation of cartilage-cells into bone-cells, while in others it appears as though the new bone is being formed outside of and gradually displacing the cartilage, which merely acts as a framework. The findings from these experiments may be interpreted as evidence in favor of either method of bone formation, and it is possible that both may play a part in the process.

Comparison of the regeneration of bone and cartilage. In the regeneration of cartilage and bone it has been shown that the perichondrium and the periosteum take an analogous part in the formation of their respective new tissues.

The periosteum is a direct derivative of the perichondrium, and the osteoblast is a direct derivative of the chondroblast. In the regeneration of bone the osteoblast tends to revert to the chondroblastic type, as is shown by the formation of cartilage in the early stages. In the regeneration of cartilage there was some evidence of the reversion of the chondroblast to the connective-tissue type of cell, as was noticed in the tissue about the new-forming cartilage.

After the periosteum has proliferated into cartilage it is rapidly transformed, either directly or indirectly, by some specific influence, perhaps of a chemical or physical nature, into bone. The cartilage, on the other hand, continues to grow as cartilage, but that it may also be changed into bone is shown by the fact that ossification occurs in cartilage in old age.

The governing and determining force is the same as that which is fundamental to all growing conditions and is dependent upon a specific property of the cell which determines the character of the tissue to be formed in each case.

III. THE REGENERATION OF CARTILAGE AND BONE AT THE CHONDROCOSTAL JUNCTION

The chondrocostal junction affords an opportunity for studying regeneration of bone and cartilage at the same time and of determining the parts that the perichondrium and the periosteum exert in the restoration of the cartilage and bone respectively.

The normal chondrocostal junction has a very close resemblance to a normal epiphysis and is affected in a similar manner in certain diseases. During the period of growth of the chest it possibly acts as an epiphysis in increasing the circumference, but after the adult period has been reached, instead of undergoing the usual changes, the cartilage persists and assumes the function of giving elasticity to the chest wall. In the anatomical description of the ribs no mention is made as to whether the chondrocostal junction is to be considered as an epiphysis. If it be granted that it acts as an epiphysis even in a limited degree, the following findings will be of especial interest.

As there are certain peculiarities of the perichondrium and the periosteum and their enclosed tissues at the chondrocostal junction, it will be necessary to give a detailed description of their structure.

At the chondrocostal junction the periosteum is seen to become thicker and to extend

over on to the cartilage for a short distance, lying beneath the perichondrium. The cortical bone becomes thinner as it approaches the junction and gradually intermingles with the cancellous bone islands. The perichondrium presents nothing abnormal at the junction, but the cartilage cells are larger and have the columnar arrangement which is characteristic of an epiphysis.

The perichondrium and the periosteum are rather adherent at the junction, and after their removal a slight thickening is seen in that region. Upon microscopical examination of the perichondrium and the periosteum, after removal, no definite particles of cortical bone can be found.

This part of the subject will be considered under the following three subdivisions:

(*a*) Regeneration of bone at the junction; subperiosteal resection of bone from the chondrocostal junction toward the rib side.

(*b*) Regeneration of cartilage at the junction; subperiosteal resection of cartilage from the junction toward the sternal side.

(*c*) Regeneration of bone and cartilage at the junction; subperiosteal resection of cartilage and bone including the junction.

(*a*) REGENERATION OF BONE AT THE JUNCTION

Method. A piece of bone from one to two centimeters in length was removed subperiosteally at the chondrocostal junction. The operations were performed with the same technique as in the previous cases.

Results. In all of these experiments there was regeneration of bone as in the ordinary resection of the rib. As there is cartilage on one side and bone on the other, it is necessary to give the microscopical findings to show the part each takes in the regeneration.

Experiment 12; Rabbit 286; 5 days.

Gross examination. The space between cartilage and bone is filled with blood-clot.

Microscopical examination. The changes are practically the same as for the regular resection. There is no proliferation at the cartilage-stump and the usual conditions are present at the angle of the periosteum and the bone. There is not quite so much cartilaginous proliferation from the periosteum as in Experiment 7.

Experiment 13; Rabbit 279; 10 days.

Gross examination. There is practically complete filling of the periosteal gutter with new tissue.

Microscopical examination. There are scattered areas of cartilage and osteoid tissue which are quite irregular in distribution. It has been claimed that the callus is all ossified from the old bone, but that such is not the case is shown by the fact that the osseous tissue near the periosteum is separated from the original bone by an intervening layer of cartilaginous and osseous tissue.

Experiment 14; Rabbit 277; 15 days.

Gross examination. The periosteal gutter appears to be filled with calcareous material.

Microscopical examination. No additional changes are noticed at this time except that there is some proliferation from the marrow and the cortex of the bone-stump. There is also a slight growth of cartilage from the cartilage-stump.

Experiment 15; Rabbit 279; 28 days.

Gross examination. There is complete regeneration of bone in the periosteal gutter.

Microscopical examination. The new tissue between the two ends is practically all osseous, and there is a beginning differentiation into the medulla and cortex. (The regeneration of the marrow will not be considered at this time.) The periosteum has assumed its normal appearance and relation to the cortex. Even at this advanced stage it is easy to distinguish the bone that has arisen from the periosteum from that which has originated from the cortex and medulla. At the place where the new bone meets the cartilage-stump there is the appearance of a normal chondrocostal junction.

Conclusions. In this series of experiments one is again impressed with the important part which the periosteum plays in the regeneration of bone. It is also noticed that there is very little tendency for the cartilage to grow over on to the periosteal bed.

(*b*) REGENERATION OF CARTILAGE AT THE JUNCTION

Method. A piece of cartilage from one to two centimeters in length was removed subperichondrially extending from the chondrocostal junction toward the sternum. On account of the form of the cartilage, it is sometimes impossible to separate it completely from the perichondrium.

Results. In the six experiments of this nature there was a different amount of cartilage regenerated according to the length of time that had elapsed. The results will be briefly given:

Experiment 16; Rabbit 276; 5 days.

Gross examination. No changes can be made out at this time.

Microscopical examination. There is a slight proliferation of all the layers of the perichondrium.

Experiment 17; Rabbit 426; 10 days.

Gross examination. There is a considerable amount of new tissue in the perichondrial gutter which appears to be cartilaginous.

Microscopical examination. There is an active growth of new cartilage between the two stumps which is definitely of perichondrial origin. There is no growth from the cartilage-stump except in the neighborhood of the perichondrium, while from the bone-stump there is some proliferation from the cancellous bone islands.

Experiment 18; Rabbit 319; 15 days.

Gross examination. The perichondrial gutter appears to be filled with fibrocartilaginous material.

Microscopical examination. The appearance is similar to that described in Experiment 17, differing only in that the process is more advanced.

Experiment 19; Rabbit 1[2]; 20 days.

Gross examination. The space between the two ends is completely filled with new cartilage.

Microscopical examination. There is a slight increase in the amount and density of the regenerated cartilage, and the greater part of it arises from the perichondrium. It is interesting to follow the changes at the bone-stump, as there appears to be a direct transformation of bone into cartilage. The bone at that place is arranged in islands which are beginning to take on a bluish tinge like cartilage. The nuclei of the bone-cells are enlarging and appear to be changing directly into cartilage-cells. In view of the fact that there is a considerable dispute as to whether cartilage-cells can change directly into bone-cells, this retrogressive change of the bone-cell to the cartilage-cell is especially interesting.

Conclusions. With cartilage at one end and bone at the other end of a strip of perichondrium the regenerated new tissue will be cartilage, but if the intervening strip consist of periosteum the regenerated tissue will be bone. Admitting that the two stumps in either condition proliferate to a slight extent, one cannot but admit that the periosteum and the perichondrium determine the character of the regenerated tissue. From the sections it is evident that the regeneration is due to a proliferation of the cellular layers of the periosteum or the perichondrium, independent of the adjoining tissue.

The next set of experiments add further proof to these assertions.

(*c*) REGENERATION OF BONE AND CARTILAGE AT THE JUNCTION

Method. The bone and cartilage were subperiosteally and subperichondrically resected so as to include the chondrocostal junction.

Results. At periods of 5, 7, 10, 13, 15, 20, 27, and 43 days there were bone and cartilage regenerated on their respective sides of the junction.

Experiment 19; Rabbit 349; 5 days.

Gross examination. Nothing but blood-clot can be seen in the intervening space.

Microscopical examination. It is interesting to note that the regeneration of bone and cartilage are going on independently on their respective sides of the junction. No additional conditions are noticed besides those previously described for each type of regeneration for this stage.

Experiment 20; Rabbit 320; 7 days.

Gross examination. Nothing definite as to the nature of the tissue in the gutter can be ascertained.

Microscopical examination. There is regeneration of bone up to the junction, at which place the new cartilage begins and extends up to the cartilage-stump.

Experiment 21; Rabbit 275; 10 days.

Gross examination. On the side toward the rib-stump there is calcareous material which becomes continuous with cartilaginous tissue at the chondrocostal junction.

Microscopical examination. At this stage there is a more advanced development of cartilage and bone on their respective sides of the junction. These two tissues meet in an irregular manner at the junction, but it looks as though there was an effort to adjust themselves to the growing forces and that they were tending to establish a condition of equilibrium.

Experiment 22; Rabbit 273; 13 days.

Gross examination. There is a heavier formation of bone and cartilage at this time, but they bear the same relative position to each other as in the previous experiment.

Microscopical examination. The appearance is similar, but is in a slightly more advanced condition than in the previous experiment.

Experiment 23; Rabbit 273; 15 days.

Gross examination. The bone appears to be completely regenerated up to the junction, from which place a tubular cartilage-like mass extends up to the cartilage-stump.

Microscopical examination. The new bone is denser than in the previous experiment, although the cartilage is found to be in irregular patches.

Experiment 24; Rabbit 427; 20 days.

Gross examination. There is a complete regeneration of cartilage and bone, the two tissues meeting at the chondrocostal junction at which place they form a bulging mass.

Microscopical examination. The bone is quite dense and is surrounded by a fairly normal appearing periosteum. The cartilage is likewise well formed and ends abruptly where the bone begins. Upon studying the place of union of this new bone and cartilage, one is impressed with its similarity to the normal chondrocostal junction (Fig. 10). There is not the exact, even appearance of the normal junction, and the cartilage has not the regular columnar arrangement; but it is possible that at a later stage the balance of growth would be adjusted and there would be a still nearer approach to the normal.

Conclusion. From the last set of experiments and the two preceding groups one must conclude that the perichondrium and the periosteum are very important factors in the regeneration of cartilage and bone, each determining the character of the tissue to be formed in its respective case.

The restoration of the chondrocostal junction is very important, especially if it is to be considered as an epiphysis. The regeneration of the cartilage and bone at that place, as determined by the perichondrium and the periosteum, and the establishment of a balance of growth are very interesting growth phenomena. Even if the chondrocostal junction in a restricted sense is to be considered as an epiphysis, its restoration is all the more striking in view of the fact that the normal epiphysis is so susceptible to injury.

The perichondrium regenerates cartilage by a direct proliferation of its chondroblastic tissue into cartilage, while the periosteum regenerates bone by an indirect proliferation of its osteoblastic tissue, first forming cartilage, which is then changed into osteoid tissue. From these sections there is considerable evidence that the cartilage-cell can change directly into a bone-cell and also that under certain conditions osseous tissue can change into cartilage by a direct retrogressive process, in which the bone-cell changes directly into a cartilage-cell. If all of these processes are possible, then it is easy to conceive of a cycle of developmental changes by which cartilage can be changed into bone and bone transformed back to cartilage. When we consider the close relationship which exists between these two tissues it does not seem improbable that some such transformations may occur.

GENERAL SUMMARY

1. The periosteum is directly and actively concerned in the regeneration of bone. In the very early stages the periosteum proliferates to form a cartilaginous tissue, which is later transformed into bone.

2. The exact method of the changes from cartilage to bone cannot be determined. There is considerable evidence in favor of the direct change of the cartilage-cell into the bone-cell. There is at times the appearance of the osteoblast forming bone and substituting the cartilage. Therefore it seems as though both processes can take place at the same time.

3. The regeneration of bone also takes place from the marrow and cortical bone, but in a more limited degree and at a later period than that from the periosteum.

4. The regeneration of cartilage takes place almost entirely from the perichondrium. It proceeds by a direct proliferation of all the layers of the perichondrium beneath the outer fibrous tissue. There is some evidence in favor of the view that the connective tissue is also transformed into cartilage under the stimulation of the neighboring cartilage or perichondrium.

5. There is a slight amount of regeneration of cartilage from the original cartilage near the perichondrium, but the remainder of the cut end tends to undergo degenerative changes.

6. The extent of the removed cartilage exerts no influence on the regeneration. (There is no evidence of calcareous changes in the regenerated cartilage, even as late as 46 days.)

(In closing I wish to express my thanks to Professor Ophüls for his advice and suggestions during the performing of these experiments.)

REFERENCES

1. Von Korff, K. Über die Histogenese und Struktur der Knorpelgrundsubstanz. Arch. f. mikr. Anat., 1914, lxxxiv, 263.
2. Matsuoka, M. Die Regeneration des Knorpelgewebes. Virchow's Arch. f. path. Anat., etc., Berl., 1904, clxxv, 32.
3. Maltesta, R. Über Knorpelheilung nach aseptischen Verletzungen am hyalinen, von Perichondrium überzogenen, fertigen Knorpel. Virchow's Arch. f. path. Anat., etc., Berl., 1906, clxxxiv, 123.
4. Axhausen, G. Über den histologischen Vorgang bei der Transplantation von Gelenkenden, inbesondere über die Transplantationfæhigkeit von Gelenkknorpel und Epiphysesknorpel. Arch. f. klin. Chir., 1912, xcix, 1.
5. Davis, S. The Transplantation of Rib Cartilage into Pedunculated Skin Flaps; an Experimental Study. Bull. Johns Hopkins Hosp., 1913, xxiv, 116.
6. Haas, S. Regeneration of Bone from Periosteum. Surg., Gynec. & Obst., 1913, xvii, 164.
7. Ryerson, E. Clinical Aspects of the Regeneration of Bone, as Manifested by a Study of the Union of Fractures. Canad. M. Ass. J., 1913, iii, 865.
8. Gallie, W., and Robertson, D. The periosteum. Canad. M. Ass. J., 1914, iv, 33.
9. McWilliams, C. The Periosteum in Bone Transplantation. Is Contact with Living Bone Necessary for the Life of Grafts, and Will Transplanted Periosteum Produce New Bone? J. Am. M. Ass., 1914, lxii, 346.
10. Groves, E. An Experimental Study of the Operative Treatment of Fractures. Brit. J. Surg., 1914, i, 438.
11. Mayer, L., and Wehner E. Neue Versuche zur Frage der Bedeutung der einzelen Komponenten des Knochengewebes bei der Regeneration und Transplantation von Knochen. Arch. f. klin. Chir., 1914, ciii, 732.
12. Brown, W. L., and Brown, C. P. Preliminary Report on Experimental Bone and Periosteal Transplartation. Surg., Gynec. & Obst., 1913, xvii, 681.
13. McWilliams, C. The Function of the Periosteum in Bone Transplantation Based on Four Human Transplantations without Periosteum. Surg., Gynec. & Obst., 1914, xviii, 159.
14. Lewis, E. J. Experimental Work on Bone Transplantation. Surg., Gynec. & Obst., 1914, xviii, 572.
15. Cohn, I., and Mann, G. Osteogenetic Function of Periosteum and Bone Transplants. Southern M. J., 1914, vii, 214.
16. Moore, J. E., and Corbett, J. F. Studies on the Function of the Periosteum. Surg., Gynec. & Obst., 1914, xix, 5.

THE CLINICAL MANIFESTATIONS OF DISEASE OF THE GLANDS OF INTERNAL SECRETION IN GYNECOLOGICAL AND OBSTETRICAL PATIENTS*

By ROBERT T. FRANK, A. M., M. D., New York City
Associate Gynecologist, Mt. Sinai Hospital

I. Introduction

THREE years ago I read a paper before this society dealing with "The Function of the Ovary."[1] To-day I propose to extend the discussion beyond the sexual tract because, in the interim, our knowledge concerning the intimate correlation between the gonads and the other organs of internal secretion has increased sufficiently to allow of at least a fragmentary survey of their interaction. The previous paper was confined to physiological observations gained in the laboratory; the theme of the present one concerns itself mainly with their clinical application in both health and disease.

Confusion exists in the literature dealing with the ductless glands, partly because apparently conflicting observations are recorded, partly because the attention of investigators has been necessarily focused upon the individual problems upon which they are engaged. The present study has resulted from an attempt to evolve a practicable working plan applicable to the clinical investigation of gynecological and obstetrical cases which show derangements of the glands of internal secretion. Although future study may necessitate radical revision of many of the views expressed, this outline may prove of use in gaining further knowledge.

It is more with the hope of pointing out methods of standardizing our researches, of utilizing the clinical material to better advantage, and consequently of attaining a clearer insight into this obscure chapter of medical science, than with the design of contributing startling new facts, that I have undertaken the writing of this paper.

The weight of evidence acquired during these last years has emphasized the fact, previously known, that the glands of internal secretion (specifically the gonads or sex glands, the thyroid, parathyroids, hypophysis or pituitary, pineal gland or epiphysis, adrenals and pancreas) form a connected chain. Dissociation of their interrelation or disturbance of mutual balance suffices to produce variations from the normal. Therefore, symptoms produced by disease, or by deliberate injury or removal of a given gland, may manifest themselves by phenomena ascribable to one or more distant members of the chain; likewise, response to therapeutic measures, though apparently the direct result of effects produced upon a certain gland, may really prove to be due to mediate action through other members of the group.

The huge and rapidly growing literature is accessible in three recent painstaking and commendable works, those of Biedl,[2] Falta,[3] and Swale Vincent.[4] Therefore, I may be pardoned in my choice of only such articles as have direct bearing upon the points requiring emphasis.

II. The Glands of Internal Secretion Regarded Individually

In order to present to you, as clearly as is possible, at least in outline, the most essential and fundamental functions currently ascribed to each gland, I have drawn up an abstract in which each gland is considered as if separate, or dissociated, from the others — though I am well aware that this arrangement is both arbitrary and open to criticism. With each gland, as far as is possible, the following points have been noted: 1. Is the gland essential for the continuance of life or health? 2. What symptoms are produced by excessive or hyperfunction? 3. What symptoms are produced by reduced or hypofunction? 4. Do the symptoms of partial or complete

[1] Frank, R. T. Surg., Gynec. & Obst., 1911, xiii, 36.

[2] Biedl, A. Innere Sekretion, Second Edition, 1913.

[3] Falta, W. Die Erkrankungen der Blutdrüsen, 1913.

[4] Vincent, S. Internal Secretion and the Ductless Glands, 1912.

* Read in Abstract at the 39th Annual Meeting of the American Gynecological Society, Boston, May 21, 1914.

removal of the gland correspond to the clinical symptoms of hypofunction? 5. Does replacement or opotherapy act as a successful substitute for the gland? I have chosen this somewhat pedantic method as the only available means of avoiding the hopeless confusion into which the entire subject has been plunged by innumerable contradictory reports.

As the theory of disfunction (i. e., qualitative change in secretion) at present rests upon no foundation admitting of proof, it has been deliberately excluded from this generalization. Wherever disturbances of the glands produce distinct and generally known symptom complexes, such complexes have been used to designate the effects, in preference to a more detailed description.

A. *Hypophysis or pituitary gland.* Composed of anterior (glandular), middle (epithelial margin), and posterior or infundibular (nervous) portion.

1. The anterior lobe is essential to life (Cushing;[5] denied by Horsley[6]). The posterior and middle lobes are not essential. 2. *Hyperfunction* produces acromegalic symptoms in adults; gigantism if developed before puberty. 3. *Hypofunction* (pressure on the infundibulum or stalk, through which the secretion is supposed to reach the system, will produce this) in adults causes adiposity (if from tumor, called "Fröhlich's syndrome") — dystrophia adiposito-genitalis[7]; before puberty, true dwarfism. 4. *Hypophysectomy* (complete removal of anterior and middle lobe or section of stalk) produces sluggishness, falling out of hair, glycosuria, emaciation, coma, death. 5. Anterior lobe extracts delay the fatal outcome, relieve the symptoms due to partial removal (Cushing). Posterior lobe extract (pituitrin) raises the blood pressure and causes contractions of the pregnant uterus, but does not ameliorate the vital symptoms.

B. *Thyroid gland.* 1. Not absolutely essential to the continuance of life, removal followed by severe symptoms. 2. Hyperfunction causes Graves' disease.[8] 3. Hypofunction in adults produces myxœdema; in infancy, cretinism. 4. Removal produces Cachexia strumipriva. 5. Thyroid extract improves cretinism and relieves myxœdema as long as the drug is exhibited.

C. *Parathyroid glandules.* 1. Probably essential to the continuance of life. 2. Hyperfunction has been said to cause osteomalacia and eclampsia; proof wanting. 3. Hypofunction produces tetany in pregnancy. 4. Parathyroidectomy is followed by tetany. 5. Parathyroid extracts are claimed to ameliorate tetany symptoms, at least temporarily.

D. *Thymus.* 1. Not essential to the continuance of life. 2. Hyperfunction (?); status thymicus and status thymicolymphaticus is so regularly accompanied by general hypoplasia of vascular system and other glands of internal secretion, and by hyperplasia of the lymph-glands, that the importance of the thymus change *per se* is questionable. 3. Hypofunction; normally involutes between the 10th and the 15th years. 4. Thymectomy; no influence in adults; transient retardation of body growth in infancy. 5. Thymus extract effects questionable.

E. *Adrenals* (cortex: *interrenal* system, mesodermal origin, rich in lipoids; medulla: *chromaffin* system, neuro-ectodermal origin, contains adrenalin). 1. Essential to the continuance of life. 2. Hyperfunction (cortical?), in adults, hypertrichosis; in infancy, precocious puberty; in utero, feminine pseudohermaphroditism (?). 3. Hypofunction (especially medullary); Addison's disease; marked aplasia in status thymicolymphaticus. 4. Adrenalectomy, muscle weakness, apathy, glycosuria, death in a few days. 5. Adrenalin and adrenal extracts from the entire gland do not prevent death.

F. *Pancreas* (islands of Langerhans internal secretory; acinous portion external secretion). 1. Essential to the continuance of life. 2. Hyperfunction unknown. 3. Hypofunction of island portion produces diabetes. 4. Pancreëctomy, glycosuria, polyuria, emaciation, and death. 5. Pancreas extracts ineffective. Recently Biedl[9] asserts that

[5] Cushing, H. The Pituitary Body.

[6] Handelsmann and Horsley, Sir V. Brit. M. J., 1911, ii, 1150.

[7] Fröhlich. Wien. klin. Rundschau, 1901, xv, 883.

[8] In recent years the thymus has been thought to play an important rôle in exophthalmic goiter. For a résumé of the literature see M. G. Seelig, Interst. M. J., 1913, xx, 078.

[9] Biedl, A. Innere Sekretion, 1913, ii, 360.

lymph (through which the pancreas secretion is supposed to be carried into the circulation) relieves symptoms of hypofunction.

G. *Pineal gland, epiphysis.* 1. Not essential to the continuance of life (Biedl,[10] Exner & Boese[11]). 2. Hyperfunction, in adults, obesity or cachexia (?); in childhood no definite effect? 3. Hypofunction, bodily and sexual precocity. 4. Pineal gland extirpation, in adults no effect (Biedl[10]); (Exner & Boese[11]) rabbits, negative; (Foà[12]) cocks, premature maturity; (Cristea[13]) retarded development. 5. Extracts (?).

H. *Ovaries* (follicles, corpus luteum, interstitial gland). 1. Not essential for the continuance of life. 2. Hyperfunction, in adults, menorrhagias; in childhood, premature sexual development. 3. Hypofunction, in adults, amenorrhœa, obesity (probably secondary); in childhood, infantilism. 4. Oöphorectomy, in adults artificial menopause; in childhood, eunuchoid habitus, genital atrophy, neuter type (no human data). 5. The reports on ovarian extracts show no uniformity of results.

I. *Metabolism.* Each of the glands appears to have some influence on metabolism. The effects are too obscure, as yet, to permit of clear exposition. In the main, metabolic activity is stimulated by the thyroid, the chromaffin system (adrenal medulla, chromaffin ganglia), and the posterior lobe of the hypophysis (extirpation reduces assimilation); the pancreas, the parathyroids, and the anterior lobe of the hypophysis decrease metabolic processes (Falta, p. 5). The activity of the adrenal cortex and ovary are doubtful. Carbohydrate assimilation depends largely upon the pancreas. Glycogen is set free under the influence of the chromaffin system. The thyroid influences the protein changes. The regulation of oxidation, mineral salt, etc., is largely a matter of speculation.

J. Our knowledge of bone growth (stimulation, retardation) and nerve influences (increased or decreased irritability, inhibition or stimulation of the vegetative system) are likewise in too chaotic a state to permit of short exposition.

This bare outline of the most striking phenomena produced by each individual gland considered as a separate entity is greatly modified by the effects of their interaction (correlation), which may increase, decrease, or neutralize their individual action to such a degree as to escape analysis in the present state of our knowledge. As this paper concerns itself mainly with the genital sphere, the sum of the action of the various ductless glands upon the organs of generation, and, reversely, the effect produced by the gonads upon these same glands, is of major importance. W. Blair Bell[14] has already attempted such a generalization.

It must be borne in mind that the genital tract reacts to all stimuli to which it is responsive in one of two ways: by an increase or by a decrease in function. On the other hand, the influence of the gonads, when regarded from this somewhat artificial viewpoint, might be expected to be more complex because it may (at least in theory) influence each individual of the ductless chain, alone or in various combinations.

The genital tract in the present connection must be regarded as composed of not only the internal and external genitals, but also as embracing the secondary sex characters, which include the breasts, the distinctive type of skeletal development (female and neuter), the fat and hair distribution, larynx, and psyche. The bony structures are but little affected after puberty; and, therefore, influences which in infancy produce striking deviations in dimensions, no longer do so after adult life has been reached.

III. Effect Produced by Ductless Glands of the Female Genital Tract

1. *Specific action.* Early involution of the thymus or destruction of the pineal gland produce premature sex development (including early body growth and feminine skeletal dimensions). Early hyperplasia of the thymus gland causes very marked genital hypoplasia and persistent infantile proportions. 2. *Specific action.* Excessive action of the

[10] Biedl, A. Ibidem, p. 195.

[11] Exner, A., and Boese, J. Deutsche Ztschr. f. Chir., 1910, cvii, 182.

[12] Foà, C. Arch. ital. de Biol., 1912, lvii, 233.

[13] Cristea, G. München. med. Wchnschr., 1913, lx, 1051; cocks after pinealectomy showed atrophic testes and less marked secondary sex characters.

[14] Bell, W. Blair. Lancet, Lond., 1913, xci, 809.

adrenal cortex may produce premature sex development. More regularly it causes excessive hair growth (often of the male type), and genital hypoplasia. 3. *Non-specific action.* The effect of either hyperfunction or hypofunction of the thyroid and hypophysis is less specific; both are eventually followed by reduced development and function of the genital tract (though often preceded by transitory stimulation. 4. *Indifferent action.* The parathyroid and pancreas produce no changes. 5. *Ovarian effects.* Tumors of the ovary *per se* may cause early sex maturity, which may regress after removal of tumor.[15]

IV. Effects Produced by the Gonads on Other Ductless Glands

The most unequivocal effects are obtained by castration. The hypophysis increases in size (anterior lobe, eosinophiles more numerous, adiposity, long extremities). The thyroid shows accumulation of colloid in rabbits (Bell[14]); in the human it may be atrophic. The adrenal cortex becomes hyperplastic (increased sensitiveness to adrenalin). The pancreas remains unchanged. (Rebaudi [16] claims that the Langerhans islets hypertrophy). The pineal gland hypertrophies. The thymus may persist unduly. The parathyroids are unaffected.

The general systemic effects of castration can be explained only in part by these numerous changes.

In infancy, in addition to the failure of genital development referable directly to the ovaries, the eunuchoid type appears (hypophysis). Other changes are still largely a matter of conjecture. The effect of castration on the metabolism is too unsettled to warrant serious discussion. Old and doubtful experiments are quoted with unfailing regularity. Complete revision of the subject is urgently needed.[17] No conclusive evidence of the effect of ovarian hypersecretion, except upon the genital tract, is available.

All that has preceded has served mainly to illustrate the complicated interrelation existing between the various members of the ductless chain. But as the changes which take place in the genital tract originate either directly in the ovary, or are transmitted through this organ, the mechanism by means of which the gonad performs its function requires detailed study. In the present state of our knowledge, the following appears true.

V. Local Genital Function of the Ovary: Physiological

The ovary cannot be regarded as a simple or homogeneous organ. Functionally its different elements appear to have different properties. The constituents of the ovary are the follicle apparatus, the interstitial gland, and the corpus luteum.

1. The follicle apparatus

The primordial ova. The primordial ova (germ cells) most probably are direct descendants of the earliest division of the fertilized ovum (blastomeres). They reach the *anlage* of the ovary by wandering through mesentery (Fuss [18]) and are here surrounded by the so-called germinal epithelium, a derivative of the lining of the cœlum, thus forming *primordial follicles.* Even during intra-uterine life a limited number of primordial follicles develop into graafian follicles; and Runge [19] reports a corpus albicans (?) in an infant two years of age.

As castration in the young animals invariably is followed, not only by atrophy of the internal and external genitals, but also by the cessation of development of the breasts and changes in the secondary sex characters (eunuchoid type), the normal development of these structures and qualities must either directly or indirectly be ascribed to the follicular apparatus — the corpus luteum being absent at this stage — unless the action of the interstitial gland (*vide infra*) governs their growth.

[15] Riedel, H. Wien. klin. Wchnschr., 1904, xvii, 942. Lenz. Arch. f. Gynäk., 1913, p. 67.

[16] Rebaudi, S. Zentralbl. f. Gynäk., 1908, xxxii, 1332. According to this author, in rabbits, after the corpus luteum is removed, the islets of Langerhans hypertrophy.

[17] The change of metabolism following castration has shown no uniform results. This is partly due to inaccuracies of experimentation. McCrudden (J. Biol. Chem., 1910, vii, 185) found no change in the metabolism of energy. He examined the intake, urine, and fæces for nitrogen, sulphur, P_2O_5, CaO and MgO. These seem the most trustworthy of all the experiments recorded. For the literature see Biedl, Innere Sekretion, Second Edition, 1913, p. 272.

[18] Fuss, A. Arch. f. mikr. Anat., 1912–13, lxxxi, Abt. 2, 1.

[19] Runge, E. Arch. f. Gynäk., 1906, lxxx, 43. Growing follicles were found in 30 per cent of ovaries before birth. Prochownik (Arch. f. Gynäk., 1881, xvii, 330) found a corpus luteum in a child 3 years of age.

Puberty is ushered in by a mighty acceleration of follicular ripening. The impulse for this change may be inaugurated by removal of the inhibitory action of the thymus and pineal gland, which involute at this period.

Whether the onset of the first menstruation is preceded by ovulation has not been settled. This mooted question can be decided only by occasional observations made at the autopsy table or at operation. The theoretical and practical importance of this question will become more apparent during the discussion of the relation of menstruation to ovulation.

The subsequent fate of ripe ova which are extruded from the ovary, become fertilized and develop in the uterus, does not concern us in this discussion, except in so far as the placenta is regarded as a gland of internal secretion by some (*vide infra*).

2. THE INTERSTITIAL GLAND

In a considerable number of mammals (about 50 per cent of those examined), complexes of large epithelioid cells are found in the stroma of the ovary (Anna Schaefer[20]). Genetically, Lane Claypon [21] derives them from the germinal epithelium (rat, rabbit); others have ascribed their origin to the stroma cells forming the theca interna of atretic follicles (Limon,[22] etc.). In the human species the interstitial gland, when present, is but slightly developed. According to Wallert [23] and Seitz,[24] it is most prominent during pregnancy (from the third month on).

The only well-developed interstitial gland encountered by me during ten years of search for this structure was obtained from the ovary of a young virgin (23 years) suffering from dysmenorrhœa and fibroids (Figs. 1 and 2).

The cells of the interstitial gland resemble those of the corpus luteum, containing similar lipoid granules.

As it has proved impossible by the most diverse experiments (X-ray, transplantation, etc.) to destroy only the follicular apparatus or the interstitial cells, without injury to the other, the question as to which of these two systems controls the growth and continued nutrition of the uterus is still unsettled.

The one observation recorded by Bucura [25] in which a minute remnant of the ovary of a rabbit sufficed to maintain uterine nutrition, the remnant examined in serial section showing only a few follicles but no interstitial cells, cannot be considered decisive without additional corroboration.

On the one hand, the fact that the follicular apparatus is constant in all species and shows distinct and traceable relations to the functional condition of the genitals (puberty, œstrus, pregnancy, climax) speaks for its functional importance; on the other, the inconstant occurrence of the interstitial gland (Schaefer,[20] Fraenkel [26]) in different, often related, species, and its apparent lack of correlation with functional states of the uterus (denied by Regaud et Debreuil [27]) make any important function doubtful. The most weighty arguments in favor of the importance of the interstitial gland are purely morphological; on the one hand is its supposed analogy to the interstitial cells of the testis (?); on the other, the similarity of granulosa and theca lutein cells (*vide infra*).

3. THE CORPUS LUTEUM

This transitory structure, which is a derivative of the follicle apparatus, now generally included among the glands of internal secretion, forms within the follicular cavity after the ripe ovum has been extruded. The corpus luteum is regularly found in all species of mammals, and occurs in pregnancy in all animals which harbor their young in the uterus. Its derivation from the epithelial cells lining the follicle (granulosa cells) is now generally conceded. The minuter details of the formation of the corpus luteum in the mouse, rabbit (Sobota [28]), guinea pig (L.

[20] SCHAEFER, A. Arch. f. Gynäk., 1911, cxiv, 491.

[21] LANE-CLAYPON. Proc. Roy. Soc. Med., Series B, 1906, lxvii, 525 (rabbit); J. Obst. & Gynec. Brit. Emp., 1907, xi, 205 (rat).

[22] LIMON, M. Arch. d'anat. micr., 1902–3, v, 155, studied histogenesis in 6 species.

[23] WALLERT. Arch. f. Gynäk., 1907, lxxxi, 271.

[24] SEITZ, L. Arch. f. Gynäk., 1905, lxxvii, 203.

[25] BUCURA. Ztschr. f. Heilkunde, 1907, xxviii, 147 (N. F. viii, Abt. f. Chir.). In this article the author also suggests that the parovarium may elaborate an important internal secretion.

[26] FRAENKEL, L. Arch. f. Gynäk., 1905, lxxv, 443, concludes that the interstitial gland cannot be credited with any general or important function.

[27] REGAUD, C., et DUBREUIL, G. Compt. rend. Soc. de biol., 1909, lxvii, 348, spring growth and sex activity increase, isolation decreases the interstitial gland. Ibid. 1908, lxiv, 217, the interstitial gland has no relation to œstrus.

[28] SOBOTA, J. Anat. Anz, 1895, x, 482.

Loeb[29]), etc., is well known for some years. Recently a great advance has been made through the careful studies of R. Meyer, [30-32] who has described not only the complete evolution of the corpus luteum in the human female, but together with Ruge [34] has correlated the stage of development of the yellow body with the coincident cyclical changes of the uterine mucous membrane, although, when he began his studies, he scouted this causal relationship.[30] As I pointed out in my previous paper, "observations made on the human species are almost negligible, partly because insufficient attention has been given to the exact age (particularly the early stages) of the corpus luteum . . ." This uncertainty no longer exists since the appearance of Meyer's work. My own material, though small in amount, corroborates the observations made by Meyer and Ruge. The question is of such fundamental importance that the results obtained by these authors must be described in detail. In order to avoid repetition, the observations of Schroeder[35] and J. W. Miller[36] and my own observations, which certainly, as far as morphology is concerned, agree with the two authors, have been incorporated in the description.

Development of the Corpus Luteum

a. *Proliferative period. Macroscopically*, immediately after ovulation the ruptured follicle appears as a small, flaccid, collapsed vesicle. This lack of prominence accounts for the fact that numerous investigators have overlooked the earliest stage. Confusion has also arisen from the gross and also microscopic resemblance of the atretic follicles to early corpora lutea. *Microscopically*, from without inward, the following conditions of the various layers is encountered. The theca externa is vascular. The theca interna contains many large, clear cells loaded with lipoid (theca lutein cells). The granulosa epithelial layer is becoming stratified (two to three layers) (Figs. 5, 6, and 7). Its cells are still small, mainly of cylindrical or spindle form, and may show mitotic division. At this stage the granulosa does not yet contain lutein or lipoid, the theca lutein cells being far more in evidence. The follicular cavity is either empty or, if the stigma is occluded, contains serum or blood.

b. *Vascularization. Macroscopically*, the corpus luteum appears as a typical bluish red prominence on the surface of the ovary. It is indistinguishable from the later stages. On cross section, more often than at a later period, the central coagulum is fluid or jelly-like in consistence and its center may be free from blood; but no absolute diagnostic value can be accorded to these differences (Fig. 3). *Microscopically*, the external thecal changes persist. The theca interna is unchanged, but appears less prominent, because of the great increase in the granulosa. The granulosa cells are considerably distended by their lipoid and lutein contents. Their nuclei are spherical and less deeply staining. The innermost layer of epithelial cells abutting on the follicle cavity have a feathery margin. Spindle-cells and red blood-cells appear at the outermost edge of the granulosa cells (henceforth to be called granulosa-lutein cells — or, briefly, lutein cells — in contradistinction to the theca lutein cells [Seitz]) where these come into contact with the internal theca, gradually forcing their way toward the follicle cavity. These isolated forerunners are followed or replaced by fine or dilated capillary vessels which everywhere penetrate between the lutein cells until they reach the follicular cavity (Figs. 8 and 9). A more or less extensive irruption of red blood-cells, varying in individual cases, takes place into the follicle cavity, which by this time has always reclosed and filled with serum or thicker fluid.

c. *Period of ripeness. Macroscopically*, the external appearance does not differ from that of the just vascularized corpus luteum. On

[29] Loeb, L. Anat. Anz., 1906, xxviii, 102.

[30] Meyer, R. Arch. f. Gynäk., 1911, xciii, 354, describes earliest stages of corpus luteum; denies relation to menstruation.

[31] Do., Ibid., 1913, c, 1. Full description of the corpus luteum genesis; acknowledges relation to menstruation.

[32] Do., Ztschr. f. Geburtsh. u. Gynäk., 1913, lxxiii, 976. further demonstration of relation of ovulation to menstruation; the ovum probably inhibits ovulation.

[33] Meyer, E., and Ruge II, C., Zentralbl. f. Gynäk., 1913, xxxvii, 50. Preliminary report.

[34] Ruge II, C. Arch. f. Gynäk., 1913, c, 20, correlation found in 106 cases (82 with regular, 24 with irregular menses) between ovulation and menstruation.

[35] Schroeder, R. Arch. f. Gynäk., 1913, ci, 1; 100 cases (69 regular).

[36] Miller, J. W. Arch. f. Gynäk., 1914, c, 1, 569. Reviews all his previous articles. According to this author, ovulation takes place 9 days before the menses. Fraenkel, L. Ztschr. f. Geburtsch u. Gynäk., 1913, lxxiv, 107.

cross section, especially toward the end of this stage, the central coagulum may be firmer, and a well-defined yellowish brown crenated margin (the lutein edge) may surround the clot. Not infrequently the center of the corpus luteum is cystic (Fig. 4). *Microscopically*, this stage is the one hitherto described as typical of the corpus luteum, the two previous stages having been generally overlooked in the human subject. The theca interna is barely definable from the externa. The large theca lutein cells have been crowded apart or have disappeared. They remain visible only in the bases of the larger septa which penetrate the lutein (granulosa) margin (Fig. 10). The lutein cells have assumed a predominant place. Their increase in size and number causes the infolding of crenation characteristic of the lutein edge. The cells are uniform, irregularly cuboidal, pale with light spherical nuclei. The cell bodies contain lipoid granules and lutein (Miller [36]). Between the cells running toward the central coagulum are innumerable straight fine capillaries, accompanied by a few spindle-cells. When these spindle-cells reach the coagulum, some spread along the surface of the epithelium, and others spread into the clot (Fig. 11). Toward the end of this period the capillary network is more prominent. Connective-tissue septa spread from the theca interna toward the centrum to meet other septa which arise from the connective tissue which has proliferated in the clot. This central connective tissue has firmly roofed off the lutein cells from the clot, which by this time is increasingly organized.

d. *Period of regression. Macroscopically*, the corpus luteum looks paler. On cross section the centrum is more solid and colorless; instead of this, the center may remain cystic. The crenated margin is of brighter yellow color, broad, and well defined. *Microscopically*, the fibrous septa are firm, the capillaries narrowed, the lutein cells smaller, vacuolated, irregularly stained, or deficient (gaps). The central core is fibrous (Fig. 12). Special stains show neutral fat in the lutein cells (Miller [36]). *Final stage of regression.* The further fibrous changes which eventually produce the *corpus albicans* are of no importance in this connection. They consist mainly in an overgrowth of connective tissue and disappearance of the lutein cells and capillaries. As final regression may extend over six or more weeks, it is not uncommon to find two, four, or more corpora lutea in various stages of regression of the ovaries.

e. *Corpus luteum of pregnancy. Macroscopically*, it is often larger than the corpus luteum of menstruation; but it cannot be differentiated from it with any degree of certainty. *Microscopically*, after the sixth or eighth week the regular arrangement of the capillary network and septa are well defined (Fig. 13). According to Miller, considerable accumulation of colloid in the lutein cells (van Gieson's stain) is characteristic; also an irregularly distributed deposit of calcium salts (Fig. 14). Fat in large quantities is absent at all times, according to Miller, regression (during the puerperium) taking place by necrosis.

4. SUBSIDIARY CHANGES IN THE OVARY

A. *Follicle atresia.* At any stage of development, the primordial or graafian follicle may degenerate (Fig. 15). Normally, this process is ushered in by the disappearance of the epithelium (granulosa), absorption of the follicular fluid, and collapse of the vesicle. The connective tissue of the thecal layers grows outward into the ovarian stroma, destroying the marginal definition of the follicle. Most characteristic is the broadening and hyaline change of the fine, almost invisible layer of connective tissue which separates the granulosa cells from the theca-lutein cells. Fine bodies of fibrillæ also enter the follicle cavity and organize within it (Fig. 17). Especially in pregnancy (Wallert,[23] Seitz[24]), the process of atresia is accompanied by well-marked lutein changes in the thecal cells (theca lutein), thus forming what these authors call the interstitial gland in the human female.

The degenerating connective tissue may form broad homogeneous bands (hyaline, staining red with van Gieson) either within or without the atretic follicle with resultant bizarre figures (Fig. 18). Large atretic follicles are usually indistinguishable, to the naked eye, from ripe follicles.

Still more recently R. Meyer [31] has described variations in follicular atresia which, unless borne in mind, may lead to confusion. As our knowledge increases, these variations may assume significance in pathology.

B. *Accessory lutein formation in atretic follicles.* The atresia is indicated by the cardinal signs (partial destruction of the granulosa), by a well-defined hyaline change in the connective tissue separating granulosa from the theca lutein cells, and by the irregular size and grouping of these thecal cells. A portion of the granulosa cells (one-twentieth to one-fourth of the periphery) are changed into true lutein cells, and show a stage of development (proliferation, vascularization, ripeness, or regression) corresponding exactly to that of the true corpus luteum, which is coincidentally present in one of the ovaries. This accessory lutein formation may be especially marked during pregnancy.

C. *Theca lutein proliferation in atretic follicles during pregnancy, in hydatid mole and chorio-epithelioma.* Either with or without the granulosa lutein changes just described, the theca-lutein cells of atretic follicles may be unusually prominent and well-developed. The fibrillar connective tissue may penetrate the thecal cells in all directions; the hyaline band is never lacking. In hydatid mole and chorio-epithelioma the great increase in theca lutein cells, combined with distention of the cavity of atretic follicles, produces the typical *lutein-cystic ovaries*, which may assume tumor-like proportions (Findley[37]); but these ovarian pseudo-tumors may regress after the uterus is emptied or removed (Fraenkel [38]).

5. CORRELATION OF OVULATION AND MENSTRUATION

The foregoing description appears to set at rest the long-mooted question as to the genesis of the corpus luteum. A further advance has been made by correlating these various stages with cyclical changes in the uterus, described many years ago by Kundrath and Engelmann [39] and rediscovered and popularized by Hitschmann and Adler.[40] Meyer and Ruge, Schroeder, and also Fraenkel [41] and Miller, differ somewhat in their interpretation of the time relation existing between ovulation and menstruation. They all agree, however, that a distinct relation between these processes can be recognized. That such relationship exists — as was long since pointed out by Fraenkel,[42] but repeatedly denied by Leopold and Miranoff,[43] and Leopold and Ravano,[44] and others — can no longer be disputed. The discrepancies arose because observations made at operation are misleading, as the just-ruptured follicles are readily overlooked, and the formed corpus luteum does not permit the operator to differentiate between earlier stages, periods of ripeness, or even of beginning regression.

Hitschmann and Adler, as will be recalled, divided the changes taking place in the uterus into four periods: (1) Post-menstrual (regressive two to three days after the menses); (2) interval (resting and early proliferative, third to eighteenth day); (3) premenstrual (marked glandular activity, eighteenth to twenty-fifth day); (4) menstrual (bleeding and deturgescence). As I have pointed out,[45] this subdivision, though undoubtedly correct, is not always demonstrable, because, on the one hand, the post-menstruum merges closely into the interval, and on the other, the interval is often indistinguishable from the early premenstruum. Different portions of the uterine mucosa, moreover, may differ, showing some variations in different areas.

The following table shows the different views held by Meyer and Ruge, Schroeder, and Miller.

Accordingly, we see that both Meyer and Ruge, and Schroeder, believe that ovulation takes place within fourteen days of the onset of the last menses.[46] Miller, basing his views

[37] Findley, P. Am. J. M. Sc., 1903, cxxv, 486; 210 cases of hydatid with cystic ovary in 8 cases.

[38] Fraenkel, L. Monatschr. f. Geburtsh. u Gynäk., 1910, xxxii, 180., 100 cases of ovarian tumors after hydatid mole are reported; of these seven are known to have regressed spontaneously.

[39] Kundrat, H., and Engelmann, G. J. Med. Jahrb. 1873, 135. Examined 217 uteri. On page 141 cyclical changes are described in detail. Their report was forgotten for many years.

[40] Hitschmann, F., and Adler, L. Monatschr. f. Geburtsh. u. Gynäk., 1908, xxvii, 1. Rediscovered the cyclical changes and showed that most of the so-called "endometritis" cases were normal conditions.

[41] Fraenkel, L. Ztschr. f. Geburtsh. u. Gynäk., 1913, lxxiv, 107.

[42] Fraenkel, L. Arch. f. Gynäk., 1903, lxviii, 438.

[43] Leopold, G., and Miranoff, M. Arch. f. Gynäk., 1894, xlv, 506.

[44] Leopold, G., and Ravano, A. Arch. f. Gynäk., 1907, lxxxiii, 566.

[45] Frank, R. T. N. Y. M. J. 1912, xcv, 627.

[46] The differences between Schroeder, and Meyer and Ruge are more apparent than real, for Schroeder's earliest stage (Plate I) corresponds to the late vascularization period of Meyer.

In two of my own cases I found corpora lutea, in the earliest vascularized stage, on the last day of menstruation.

Corpus Luteum	Uterine Mucosa	Days from Onset of Last Menstruation		
		Meyer and Ruge	Schroeder	Miller
		82 cases	69 cases	0 cases
1. Ripe follicle Corpus luteum Regressing	Menstruating to interval	1–13 days	1–14 days	
2. Rupture (ovulation) Proliferation	Interval	1–14 days	15–20 days	18th
3. Vascularization	Premenstruum	10–16 days	15–20 days	
4. Ripe corpus luteum	Premenstruum, Menstruating	16–28 days	18–28 days	

partly on theoretical considerations, partly on discrepancies he finds in Meyer and Ruge's papers, but mainly upon the purely macroscopic (operative) findings of Fraenkel, concludes that ovulation occurs on the eighteenth day in women with a four-weekly cycle, on the eleventh in those with a three-weekly cycle.

A. *Practical importance of determining the date of ovulation.* Miller correctly suggests that the exact determination of the time of ovulation has an important bearing on the success of artificial insemination. Although this procedure has not as yet attained much importance in gynecology and obstetrics, it has long ago proved of economic value among animal breeders who distribute the semen of valuable stallions, or impregnate refractory females of various species, by these means. Rohleder,[47] who has collected the literature bearing on human artificial insemination, and Hirsch [48] both place the optimum time as immediately after the period, or in exceptional cases during the last day of menstruation. The knowledge of the exact date of ovulation would also prove of value in assisting fertilization, by regular coitus, in cases of "relative" sterility.

B. *Duration of pregnancy.* The exact time of ovulation would prove of greater importance in determining more exactly the time of fertilization in normal pregnancy. This would obviate to a degree the present annoying uncertainty familiar to the obstetrician, which prevents him from predicting the time of labor with any degree of certitude, unless the current conclusion, that the duration of pregnancy is not determinate (270 to 300 days), proves true. The importance in medicolegal practice need not be emphasized.

In this connection the attempt of Bryce and Teacher [49] to determine the date of fertilization by means of the eleven youngest ova recorded in the literature is of interest. The data at their disposal are, however, not unimpeachable. From their table it appears that fertilization may take place at any time between the fifth and the twenty-fifth day after the onset of the menses. Ovulation supposedly takes place approximately twenty-four hours before this. Mall (in Keibel and Mall's Handbuch,[50] basing his deductions upon the large statistics of Ahlfeld,[51] Issmer, [52] and others, and upon a large series of embryos, concludes that impregnation usually dates from within the first week following menstruation.

Evidently, in the present state of our knowledge, we are as yet justified in concluding merely that *ovulation follows menstruation*, and that the *fertilized ovum dates from before the missed period.*

In order to clear up this much disputed point, future investigators must state definitively in their reports the type of cycle (three- or four-weekly) and the duration of the period (one to seven or more days), and should not fail to put on record all cases in which pregnancy can be traced to a single coitus of which the date and relation to the menstrual period is known.

In view of these newer acquirements, allow me to repeat and amplify the conclusions deduced in my previous paper concerning —

6. THE PHYSIOLOGICAL SIGNIFICANCE OF THE GENITAL FUNCTION OF THE OVARY — SUMMARY

A. *Prepuberty conditions.* 1. In infancy and childhood the follicle system (perhaps also the interstitial gland as represented in

[47] ROHLEDER, H. Die Zeugung beim Menschen, 1911. Reports 6 cases with 1 success. From the literature he has collected 65 cases with 21 successes.

[48] HIRSCH, J. Berl. klin. Wchnschr., 1912, xlix, 1361; reports 6 successful cases.
IWANOFF, E. Arch. de Soc. Biol., 1907, xii, 377; gives a full report on artificial insemination in animals.

[49] BRYCE, T. H. and TEACHER, J. H. Contributions to the study of the Early Development and Imbedding of the Human Ovum. 1908, page 58.

[50] KEIBEL and MALL. Handbuch der Entwicklungsgeschichte des Menschen, 1910, i, 185. From 1,200 cases, with date of impregnation known, the average duration is 269 to 271 days.

[51] AHLFELD. Monatschr. f. Geburtskunde, 1869, xxxiv, 180–266. Five hundred cases with impregnating coitus known — 26.5 per cent conceived on the last day of the menses, 72.8 per cent during first week following menstruation; average duration 269 days.

[52] ISSMER. Arch. f. Gynäk., 1889, xxxv, 310, average 268 days.

the human beings by the theca lutein cells of atretic follicles, [Wallert, Biedl, and others]) governs the growth and development of the internal and external genitalia.

B. *Cyclical conditions.* 2. At puberty, ovulation takes place; the corpus luteum secretion sensitizes the uterus, which therefore undergoes the premenstrual cyclical change, which terminates with menstruation [53] (at the time the corpus luteum regresses and loses its secretory activity; i. e., its power to inhibit menstruation [L. Loeb[54]]). 3. As soon as the corpus luteum becomes inactive, a new follicle begins to ripen, in time ruptures, and again forms a corpus luteum.

C. *Pregnancy conditions.* 4. If, after ovulation, the escaped ovum is fertilized and reaches the uterus, which by this time is sensitized by the corpus luteum and, therefore, is ready to respond by decidua formation (maternal placenta of L. Loeb[55]), nidation or embedding takes place. 5. The stimulus exerted by the products of conception in turn react upon the corpus luteum and protract its period of activity to the termination of pregnancy (R. Meyer), entailing inhibition of further follicle ripening and ovulation throughout pregnancy (Fraenkel, Loeb[54]).

D. *Climacteric conditions.* 6. As the result of lessened functional activity (whether local ovarian; secondary to other glands of internal secretion; in some cases, perhaps, as the result of consumption of all the ova), follicle ripening terminates, no copora lutea are formed, and menstruation definitely ceases.

E. *Accidental conditions.* 7. Operative removal of the corpus luteum disturbs the menstrual cycle. If the ripe follicle or the early corpus luteum is ablated, menstruation is delayed (Fraenkel [42]) by the time required for the new follicle to ripen, rupture, and form a corpus luteum. 8. Operative removal of a fully developed corpus luteum (which has already produced sufficient premenstrual change in the uterine mucosa) causes an earlier appearance of the menses (Vertes [56]). 9. Operative removal of the corpus luteum in the early weeks of pregnancy (probably second to sixth or eighth week) produces abortion or absorption of the products of conception (Fraenkel,[42] L. Loeb [57]). Considerable literature has accumulated pointing to the fact that in human beings pregnancy may continue after removal of the corpus luteum.[58]

F. *Lactation.* The condition of the ovaries during lactation amenorrhœa, and lactation atrophy of the uterus, is practically unknown. It should be the task of every gynecologist and pathologist to record the gross appearance of the ovaries and the presence or absence of a recent corpus luteum in all such instances available. Whenever possible, both uterus and ovaries should be submitted to microscopic examination.

Ovulation in most animals takes place immediately post-partum. It may do so in the human being, and conception is possible under these circumstances (conception four days post-partum [Krönig[59]]). Fertility during lactation amenorrhœa is reduced especially in the earlier months (Weinberg[60]). Permanent

[53] Occasional reports of menstruation after *complete* removal of both ovaries are not convincing. If the oöphorectomy is performed for inflammatory disease, minute ovarian rests may be left behind; accessory ovaries may be present, and I have reported a case with three ovaries (Frank, R. T. Surg., Gynec. & Obst., 1909, viii, 1) in which the third ovary might readily have been overlooked. The literature of "menstruation without ovaries" will be found in the articles by G. Gellhorn, Zentralbl. f. Gynäk., 1907, xxxi, 1195; and P. Findley, Trans. Am. Gynec. Soc., 1912, xxxvii, 82.

Landrum, S. H. J. Am. M. Ass., 1912, lix, 292. Three cases of menstruation after oöphorectomy.

[54] Loeb, L. Deutsche. med. Wchnschr., 1911, xxxvii, 17. By removing the corpus luteum in guinea pigs he found that the next œstrus occurred at an earlier date. The corpus luteum, and not the pregnancy, inhibited the growth of other follicles.

[55] Loeb, L. J. Am. M. Ass., 1909, liii, 1471.

[56] Vértes, O. Gynäk. Rundschau, 1912, vi, 289. Records 67 cases. If oöphorectomy was performed more than 12 to 13 days after the onset of the last menses, the next menstruation occurred earlier; if before the twelfth day, menstruation was postponed. The explanation given in paragraph 8 would account for these findings.

[57] Loeb (see [55]) explains the failure of nidation, by the fact that the uterus is unable to react and form the maternal portion of the placenta, after the corpus luteum has been removed.

[58] Neu, M. Zentralbl. f. Gynäk., 1911, xxxv, 392.
Löwenstein, L. Med. Klin., Berl., 1910, vi, 426 and 465.
Orgler, E. Arch. f. Gynäk., 1912, lxv, 126.
Puech, P., et Vanverts, J. Rev. mens. de Gynec., d'Obst. et de Pediat., 1913, viii, 236.
The reports are conflicting and incomplete. In many, when a single oöphorectomy was performed, no record was kept as to whether the ablated ovary did or did not contain a fresh corpus luteum. In Puech and Vanverts's paper, of twenty-five cases, six aborted; of these six, only one was beyond the eighth week of pregnancy. Three cases respectively in the fourth (?) (Essen Möller, Zentralbl. f. Gynäk., 1904, xxviii, 869), sixth, and seventh week continued undisturbed. Of Orgler's 148 cases only nine were in the second month; of these three aborted, but only one was after double oöphorectomy.
In my own experience oöphorectomy after the eighth week, even when the corpus luteum is ablated, has no effect. Before this, abortion is almost the rule; it begins late, eight to twelve days after operation. Cases with adhesions, or where intraligamentary cysts which require much manipulation are removed, must be excluded, as the trauma alone may cause the abortion, even though the pregnant uterus is notoriously tolerant (myomectomy in pregnancy).

[59] Krönig. Zentralbl. f. Gynäk., 1893, xvii, 455.

[60] Nearly half of all women menstruate throughout lactation (Creutz, see Schmidt's Jahrb., 1911, cccxii, 209). Fertility is greatly reduced in the early months, if lactation amenorrhœa exists (Weinberg, Ztschr. f. Geburtsh. u. Gynäk., 1903, l, 7).

amenorrhœa has been known to occur (Thorn.[61]) The causes which activate the breast are in dispute,[62] and, reversely, the means by which lactation reacts on the genital sphere are also not understood.

VI. Local Genital Function of the Ovary: Pathological

The previous discussion has dealt, in the main, with the morphology and function of the ovary under normal conditions, although some types of lactation atrophies verge perilously close to the abnormal. In what follows an attempt will be made to treat of the same topics in disease. On account of absence of reliable data our knowledge is most incomplete.

1. INFLAMMATORY CHANGES

A. *Acute.* The grosser type of lesions such as *acute inflammatory involvement of the ovary* (almost invariably accompanied by inflammation of the tubes, and often of the uterus and pelvic connective tissues) may not interfere with the regularity of the cyclical phenomena. Usually, menstruation is more profuse (perhaps purely local congestion and stasis). Frequently, prolonged or irregular menstruation occurs. Data are wanting to show whether this is due to changes in the periodicity of ovulation, or in irregularity in the formation and persistence of the corpus luteum.

B. *Chronic inflammatory lesions of the ovary.* Chronic inflammatory lesions of the ovary show similar variations. The wonderful resourcefulness of nature is demonstrated in advanced destructive processes, in which a minute remnant of functionating ovarian tissue suffices to continue the periodic genital function, either normally or with some variations.

When such variations do occur they usually take the form of hyperfunction, as is demonstrated not only by the accompanying menorrhagias and metrorrhagias, but by the hyperplastic conditions of the endometrium (which must be considered secondary to ovarian overactivity in those cases in which no signs of inflammation can be demonstrated). The macroscopic and microscopic appearance of the ovaries, aside from the evidences of inflammation, is so varying that no safe deductions can be drawn. Until a clearer conception of the normal processes is at our disposal, small hope of clarifying this perplexing problem can be entertained.

The importance of a thickened albuginea and microcystic degeneration of the ovaries, in this connection, need not be seriously considered (except in their relation to functional sterility — in the inflammatory type of cases the sterility is mechanical, primarily due to gross tubal lesions), because, as will be shown later, scanty and infrequent menstruation is the characteristic of this ovarian change.

2. FUNCTIONAL DISTURBANCES

A. *Hyperfunction*

a. *Metritic type.* Clinically often indistinguishable from inflammatory conditions are those of persistent menorrhagias and metrorrhagias for which no sufficient anatomical basis can be found. The gap between this pure type of functional disturbance and the inflammatory varieties is bridged by the numerous cases in which a much-thickened uterine wall is encountered — the metritic changes emphasized by Theilhaber.[63] The explanations offered by this and other authors are not the sole ones possible, because age changes, repeated childbirths, or continued ovarian hypersecretion may just as logically account for the connective-tissue increase, the sclerosed vessels (Findley[64]), the muscle changes (Anspach[65]), etc.

b. *Type without anatomical basis.* Such explanation certainly does not apply to the rarer cases in which both uterus and ovaries are absolutely normal, as appeared to be the case in two instances in which I subjected these organs to the most thorough and complete microscopic examination. The supposed ovarian changes reported by Kaji[66] have not stood the test of serious criticism.[67]

[61] Thorn, W. Volkmann's Samml. klin. Vort., 1910, No. 602–603 (Gyn. No. 218–219). Die Laktationsatrophie des Uterus.

[62] Frank, R. T., and Unger, A. Arch. Internal Med., 1911, vii, 812; also Frank, R. T., Arch. f. Gynäk., 1912, xcvii, 183; Biedl., Innere Sekretion, ii, p. 241. The fœtus, placenta, and corpus luteum have been held responsible for the pregnancy growth of the breasts. Possibly several of these factors act together.

[63] Theilhaber, A. Blutung und Ausfluss aus dem Uterus; ihre Ursachen und Behandlung, 1909.

[64] Findley, P. Am. J. Obst., 1901, xliii, 30.

[65] Anspach, B. M. Am. J. Obst., 1906, liii, 1.

[66] Kaji. Monatschr. f. Geburtsh. u. Gynäk., 1910, xxxii, 427.

[67] Pankow, O. Monatschr. f. Geburtsh. u. Gynäk., 1911, xxxiii, 339. Severely criticizes Kaji's work asserting that the changes described are physiological.

Schickele [68] takes the view that the ovaries are inactive in many cases of menorrhagia and metrorrhagia. Such cases, however, judging by my experience, must not only be exceptional, but are characterized by other symptoms, which assist in their differentiation.[69] A case of almost continuous uterine bleeding throughout many years, accompanied by abnormal increase in fertility, is of interest in this connection.[70]

Here, also, purely secretory changes, or minute variations in follicle ripening, corpus luteum formation and follicle atresia (interstitial gland), as yet not to be detected, may be the cause.

B. *Hypofunction*

a. *Amenorrhœas.* Sharply to be distinguished from the true varieties of genital aplasias with amenorrhœa are those cases of amenorrhœa in which ovulation must persist (at least in some modified form) because pregnancy takes place.[71] This may occur in extreme youth, before the onset of menstruation (see Lenz[15]), or in later life, as the following case demonstrates.

A striking instance of this class was an Italian woman of 28. Her first menstruation occurred in her nineteenth year. She married at 20, had a child when 21. The second menstruation took place at 25. Her second child was born two years later. Although she menstruated only twice, no abnormalities, either general or local, could be found. In type she was feminine. Her mother menstruated three times during her whole life.

Similar cases are reported in the literature.[72]

b. *Amenorrhœa and atrophy of uterus.* The finer anatomic changes in the ovaries and uterus which accompany and produce the genital aplasia and hypofunction due to wasting systemic diseases, such as tuberculosis, diseases of the glands of internal secretion such as acromegaly, hyperthyroidism or hypothyroidism, Addison's disease and simple (?) obesity (*Mastfettsucht*) have not been studied, so far as I am aware.

c. *Infantilism and amenorrhœa.* Herrmann [73] reports that in genital aplasia due to status lymphaticus the ovaries are enlarged in 58 per cent of the cases, and show microcystic changes, thickened albuginea, increase of the ovarian stroma, and diminution of the primordial follicles. The systemic changes characteristic of infantilism and status lymphaticus were present. They require no special mention here.

d. *Sterility.* Sterility, *per se*, certainly is a hypofunctional condition of the genitals, because the main *raison d'être* for this tract is the function of reproduction. Reynolds [74] has treated this subject exhaustively. The sterilities due to mechanical factors require no discussion in this paper.

In regard to fecundity, women may be divided into four types — the abnormally fertile, the normally fertile, the transiently sterile, the permanently sterile.

The abnormally fertile not only conceive readily and frequently, but also show a marked tendency to multiple pregnancies.[70] The ovaries evidently ovulate regularly or more frequently and prolifically than normal, but, likewise, the facilities for nidation must be exceptionally good. Anatomically, no distinctive marks are known.

The normal physiological type requires no further consideration.

The transiently sterile may be subdivided into two groups. The first shows no abnormality except a small, flaccid uterus. In this class belong lactation atrophies and atrophy secondary to systemic disease or obesity. Surprising improvement may occur within the course of a short period of time, and subsequent pregnancy is by no means uncommon. The second class, which includes milder degrees of infantilism (short vagina, shallow

[68] SCHICKELE, G., and KELLER, R. Arch. f. Gynäk., 1912, xcv, 586.

[69] Cases are met with in which persistent menorrhagia and metrorrhagia develops with obesity, small thyroid and scant hair growth. These cases are perhaps due to ovarian hypofunction, but they form a very small class. No examination of the ovaries of such cases has been made.

[70] BERGER, B. Zentralbl. f. Gynäk., 1914, xxxviii, 367. The patient was 45 years old. Her menses began at 10 years, and bleeding continued without intermission for 10 years. She conceived the day after marriage and during 25 years was pregnant 30 times, bearing 36 children, of which 20 were born alive (4 pairs of twins, one pair of triplets). Whenever the patient was not pregnant she bled continuously. The local and general examination showed normal conditions.

[71] The amenorrhœas in question are of the permanent type. It is well known that transitory amenorrhœa develops from change of climate, nervous shocks (as fear of impregnation) malnutrition. Their pathology is quite unknown. Sometimes it is impossible to distinguish between the two types, and frequently the treatment is credited with a cure, when time alone has brought about the change.

[72] HOOVER, A. R., and MARSDEN, J. K. Surg., Gynec. & Obst., 1911, xii, 288. A patient 40 years old, never menstruated, eleven children; also same for grandmother; mother menstruated once every one to two years. Blankingship, O. F., J. Am. M. Ass., 1912, lviii, 550.

[73] HERRMANN, E. Zentralbl. f. Physiol., 1909, xxiii, 265.

[74] REYNOLDS, E. J. Am. M. Ass., 1913, lx, 93.

fornices, conical cervix, short sacro-uterine ligaments), is usually not to be differentiated from the permanent sterilities. In this group surprises are frequently met with, pregnancies occurring after years of barrenness without treatment or apparent cause. These patients show a tendency to abort in their first pregnancy about the second or third month.

The permanently sterile may show no variation from the normal type. The great majority, however, are recognized by infantilism of the internal genitals (*vide ante*) accompanied by other general signs of infantilism (asexual or neuter pelvis — high symphysis, funnel-shaped outlet — and often heterosexual hair distribution, small breasts and nipples, etc.). The prognosis in these cases is almost hopeless. These sterilities may be due either to ovarian, uterine, or combined ovario-uterine deficiency, either congenital or functional in origin.[75]

Anatomically microcystic ovaries are not uncommon in these conditions. Reynolds [74] reports success attending wedge-shaped excision of the ovaries. He likewise relieved sterility by excising "persistent" corpora lutea, attention to which was first drawn by Tandler,[76] and which, as I pointed out in my previous paper, should be considered as a possible cause. No other ovarian changes have been regularly noted, except those described by Herrmann.[73] Either primarily, or secondarily through the other ductless glands, the ovaries are at fault, because the uterus (unless completely atrophic [?]) responds quickly to ovarian stimuli by hypertrophy of its muscle and hyperplasia of its mucosa.

Even if ovulation should take place, unless corpus luteum formation is physiological the fecundated ovum would probably fail to gain a foothold in the uterus. To test this deduction, I have subjected six "sterile" patients, all of whom fell into the clinical class of "dysmenorrhœa, antiflexion, and sterility," but showed few other abnormalities, to a variation of L. Loeb's experiment for the production of maternal deciduomata (which has, quite unconsciously, been performed for many years by gynecologists).

A long stem pessary was introduced through the cervix well up to the uterine fundus, different periods in the menstrual cycle being selected in each case. After seven to ten days had elapsed a curettage (and Dudley trachelorrhaphy) was performed, and the curettings were examined in serial section in order to determine whether "deciduomata" had been formed, in response to the mechanical stimulus. All the results were negative.

These results are not conclusive, because, on the one hand, Loeb's reaction may be confined to the lower animals (though not solely to rodents, as I was able to obtain it in a carnivorous species — the cat), and on the other, *sterile* patients may give no, or only a slight, reaction.

In the near future I hope to extend this method of investigation (which would prove of value also in ascertaining the time of ovulation) to patients before the performance of hysterectomy (for instance, for fibroids), because complete examination of the uterus must simplify the histological examination.

VII. Clinical Manifestations: Local and General

The interrelation of the glands of internal secretion, the detailed description of the physiological and pathological genital function of the ovary, and such scant data as are available in regard to the anatomical changes in the ovary and uterus were described in detail because, without this preliminary, intelligent discussion of the clinical manifestations is impossible. But in order to avoid needless repetitions, it will prove sufficient in most instances to mention well-known symptoms or sympton-complexes without further elaboration, and, as many of the topics have been dealt with sufficiently in what has preceded, detailed description is unnecessary.

The clinical manifestations, just as the anatomical ones, naturally fall into two groups: the hyperplastic and the hypoplastic, evidenced by phenomena of plus or minus function.

1. Genital Inactivity (Hypofunction)

A. *Congenital Conditions*

Congenital conditions such as true infantilism, however, must be placed in a class by themselves, according to Falta,[3] because the defect, which arises, so to speak, *ab ovo*, may be multiple, affecting different glands of internal

[75] Personally, I feel sure that the ovaries are the main factors. The usual causes of infantilism, especially persistent thymus, must be considered as a primary influence working through the gonads.

[76] Tandler, J. Wien. klin. Wchnschr., 1910, xxiii, 459.

secretion simultaneously, in such a way as to defy analysis and detection.

In this latter class I should also be inclined to place more marked defects such as anencephalous monsters with aplastic cortex of the adrenals [77] and genital defects, and feminine pseudohermaphroditism with adrenal hyperplasia,[78] the etiology of neither being determinable because of our present lack of knowledge. Clinically, an exact classification cannot always be carried out.

B. *Apparently Primary*

Upon careful consideration, the experienced gynecologist must realize that he has seen few cases, classifiable under this heading, which do not show abnormalities pointing to disturbance in other glands of internal secretion. Usually, when such are absent, the case will prove to be of mechanical origin (tumor substitution, inflammatory destruction, etc.). Whether the disturbance is primary in the ovary or secondary to distant trouble does not always become apparent.

a. *Local symptoms.* Stripped of all unessential details, there remain referable to the reproductive sphere these symptoms: genital hypoplasia or atrophy; scant, irregular, or absent menstruation; dysmenorrhœa; and sterility. No satisfactory explanation for the dysmenorrhœa has been obtained. One or all of these cardinal symptoms may be present.

b. *Nervous type.* The accompanying nervous symptoms are too protean to permit of description. In the main they fall under two headings (including both the psychic and general nervous functions), the stabile (stolid), and labile (high-strung) types. Both are often accompanied by sufficient evidence (small thyroid, obesity, thick skin, or slightly enlarged thyroid, tachycardia, tremor) to point to thyroid derangement.

c. *Secondary sex characters.* Defects or changes in the secondary sex characters occur frequently. They take the form either of the adult eunuchoid type (hypophyseal ?), or show a tendency toward male characteristics (species type of Tandler and Grosz [79]) (adrenal or hypophyseal overactivity ?).

1. *The adult eunuchoid type* (Tandler and Grosz) shows poorly developed breasts and nipples, deficient pubic and axillary hair, and scant accumulation of fat in the region of the lower abdomen and about the nates in thin patients, or obesity in others.

2. *The male type* has abundant hair in the axillæ, on the perineum and mons (with the male distribution — triangle with apex toward the umbilicus), coarse features, deep voice, and usually, as these patients are thin, lack of feminine fat distribution. Sometimes they verge toward the acromegalic.

3. *Abnormalities of the bony skeleton* — long extremities, pelvic anomalies (acute pubic arch, high symphysis, projecting sacrum) — point toward the fact that the process has begun before puberty. Persistent infantile proportions are characteristic of true infantilism, which many authors regard of congenital origin. (For further details see Tandler and Grosz, Falta.)

d. *Vasomotor symptoms.* Vasomotor symptoms (sweats, flushes, dizziness, etc.) are so distinct from the general nervous phenomena as to be worthy of special mention. They are most marked in the climacterium and post-operative (artificial) menopause. According to Schickele,[80] they are accompanied by arterial hypertension, but further proof must be adduced that this is not merely the physiological sequel of advancing age or premature senility.

e. *Other changes.* Variations from the normal have been noted in sugar assimilation, blood picture, coagulation time of the blood, blood constituents and response to drugs, at present not clearly defined but deserving of further study as possible means of diagnosis.

1. According to Stolper,[81] decreased sugar tolerance (glycosuria after 100 gms. of grape sugar — action probably due to disturbance of pancreas-adrenal interrelation).

[77] Meyer, R. Virchow's Arch. f. path. anat. etc., Berl., 1912, ccx, 158, considers the brain defect primary. The adrenal cortex is deficient, the medulla unaffected. In one instance a dicephalous monster (one side anencephalous, the other with well developed brain) showed complete absence of the adrenals.

[78] Auvrey. Rev. de Gynéc., 1912, xviii, 353. Usually the internal genitals are female, the external male in type.
Glynn, E. Quart. J. Med., 1912, v, 157. These pseudohermaphrodites regularly have prostates.

[79] Tandler, J., and Grosz, S. Die biologischen Grundlagen der sekundären Geschlechtscharaktere, 1913.

[80] The teachings of the Th. H. van der Velde (Über den Zusammenhang zwischen Ovarialfunktion, Wellenbewegungen und Menstrualblutung, 1905) that in each menstrual cycle many physiological functions — such as pulse, respiration, temperature, blood pressure, muscular strength, metabolism, etc. — become more active as the menses approach, and then suddenly become depressed, have been disproved. Such waves ("Wellenbewegungen") do not occur. For the literature see Schmotkin, Arch. f. Gynäk., 1912, xcvii, 395; and Viville, ibidem, 511.

[81] Stolper, L. Gynäk. Rundschau, 1913, vii, 93.

2. Blood picture changes — neutrophile leucopænia and relative lymphocytosis (Heimann [82]) (probably acting through the thymus, its value being decreased by the occasional occurrence of a similar change in ovarian hyperfunction); decrease in the eosinophile leucocytes (Adler[83]), the opposite said to obtain in conditions of hyperfunction.

3. Coagulation time is increased (Adler [83]); probably a thyroid effect.

4. Increase of blood lipoids (total fat, cholesterin, and cholesterin esters [Lindemann [84]] ascribed to the adrenals.

5. Change to drug reactions. (*a*) According to Adler,[83] increased adrenal sensitiveness, especially glycosuria in response to subcutaneous doses of 0.2 to 0.3 g. of $^1/_{00}$ adrenalin) though Keller [85] says the effect is variable. (*b*) Reduced pilocarpine effect (Adler[83]), the opposite applying to ovarian hyperfunction.

C. *Surely Secondary*

The local genital findings are as in the previous class, but unmistakably secondary to thyroid disease (Graves disease — often after a transitory stage of ovarian hyperactivity — cretinism, myxœdema), hypophyseal disturbances (acromegaly, Fröhlich's syndrome — dystrophia adiposo-genitalis), destruction of the adrenals (Addison's disease), or thymus persistence (status thymolymphaticus and infantilism). The symptoms of the primary affection usually overshadow the secondary genital changes completely.

2. GENITAL OVERACTIVITY (HYPERFUNCTION)

With few exceptions (as is to be anticipated from the fact that the activity of the sexual organs begins at puberty), symptoms of hyperfunction do not manifest themselves before puberty. Moreover, except in the cases of congenital affections, little effect on the interrelation with other glands of internal secretion becomes manifest because the growth changes are completed before the onset of the malady, although such interaction may become apparent as the result of more intensive study. The most striking symptoms are menorrhagias and metrorrhagias, which may produce secondary manifestations due to the continued loss of blood.[86]

A. *Congenital conditions.* The rare cases of precocious menstruation,[87] precocious puberty, and precocious bodily development show distinct effects produced on the entire system of ductless glands (bone growth, early ossification of the epiphyseal cartilages, well-developed secondary sex characters). Menstruation has begun as early as the third month after birth; pregnancy has occurred in the sixth year (see Lenz,[15] Hofstätter,[88] Gegenbach[89]). Psychically, the patients are childlike, often backward. At autopsy the genitals of these patients are found to be similar to those of adults. There may be no pathological findings; occasionally ovarian, pineal (usually in males), or adrenal (cortex) tumors have been noted — in the last instance male secondary sex characters predominate: hirsuties, hypertrophic clitoris. When due to ovarian tumors, regression to the normal (except such fixed changes as bone growth) may take place after oöphorectomy.[15]

B. *Puberty conditions.* The effect of early puberty as noted in individuals from Oriental races shows itself in the early ossification of the epiphyseal cartilages with resulting short stature (short arms and legs, long body).

In individuals otherwise normal, severe menorrhagias and metrorrhagias may manifest themselves at this time of life. The local examination detects no abnormality. The uterine mucosa regularly shows hyperplasia of the cystic type. Reports on the condition of the ovaries are lacking.

[82] HEIMANN, F. München. med. Wchnschr., 1913, lx, 2829.
DIRKS, M. Arch. f. Gynäk., 1912, xcvii, 583.

[83] ADLER, L. Arch. f. Gynäk., 1912, xcv, 349.

[84] LINDEMANN, W. Ztschr. f. Geburtsh. u. Gynäk., 1913, lxxiv, 819, studied the total fat, cholesterin, and cholesterin ester in normal women, amenorrhœa, and pregnancy.

[85] KELLER, R. München. med. Wchnschr., 1913, lx, 2162.

[86] In note [69] the fact has been mentioned that there may be a small class in which *hypofunction* is accompanied by hæmorrhage. One such case now under treatment has bled almost constantly since the onset of puberty (now 28 years old). She is obese, has scant hair, infantile pelvis, a small thyroid. There is leucopænia and relative lymphocytosis. The sugar tolerance and coagulation time have not yet been tested. The genitals are slightly hypoplastic. During the last three months free periods of three weeks' duration, followed by seven days of bleeding, have occurred.

[87] In passing, the transitory hyperplasia of the uterus and ovaries noted in the new-born should be mentioned. This activity is supposedly due to the mother's ovaries. Note of such occurrence in children of mothers upon whom a double oöphorectomy has been performed during pregnancy would be of value, because they would tend to prove Halban's contention (Halban, J. Arch. f. Gynäk., 1905, lxxv, 353) that the placenta and not the ovary is the activator.

[88] HOFSTÄTTER, R. Zentralbl. f. d. Grenzgeb. d. Med. u. Chir., 1913, xvi, 37. Also gives very full literature on secondary sex characters.

[89] GEGENBACH, F. P. J. Am. M. Ass., 1913, lxi, 563.

C. *Adult conditions apparently primary.* These conditions have been discussed under the heading of the *Local Genital Function of the Ovary.* The patients are usually otherwise normal, except in the "metritic type," in whom an enlarged uterus may be felt. The endometrium from these cases is usually reported by the pathologist as "hyperplastic endometrium." Sehrt [90] in thirty-five cases found the coagulation time decreased, ascribing this change to thyroid inactivity, and sustaining his contention by success with thyroid therapy. All these cases must be sharply distinguished from those due to general circulatory disease, pelvic inflammatory trouble, syphilis, etc.

D. *Preclimacteric conditions.* The same symptom-complex occurs about the climacterium. The "metritic type" predominates. Early cases of carcinoma of the body of the uterus or fibroids [91] may give the same symptoms.

E. *Secondary conditions.* Quite rarely, in the early stages of Graves' disease, acromegaly, and after thyroidectomy for goiter, transitory menorrhagias and metrorrhagias occur. This hyperactivity is followed by the more regularly occurring aplasia.

3. CONDITIONS OF HYPOFUNCTION OR HYPERFUNCTION IN PREGNANCY

A. *Does the Ovary Functionate in Pregnancy?*

No unanimity of opinion as to the functional condition of the ovaries in pregnancy exists. The weight of evidence is about equal. The uterine findings are complicated by the presence of the ovum. We now know that pregnancy can continue undisturbed, and be followed by a normal puerperium after removal of both ovaries, at least as early as the sixth week of gestation.[58] As many authors (Halban,[87] Starling,[92] Shickele,[93] Fellner,[94] etc.) ascribe distinct secretory properties to the placenta or fœtus or to a combination of both,[95] these new factors obscure the issue. The evidence obtained from clinical and experimental reports is contradictory.

A very complete and impartial review of internal secretion as modified by pregnancy is presented by Seitz,[96] who believes that the follicle apparatus is less active, ascribing importance to the interstitial gland during pregnancy.

Were the effect not marred by the possible function of the placenta and fœtus, the following evidence would point to ovarian hypofunction: decreased sugar assimilation, marked increase in size of the hypophysis (though different from that after castration — chromophobic pregnancy cells), cessation of ovulation. On the other hand, persistence of the corpus luteum, decrease of a persistent thymus, cure or improvement of pregnancy, osteomalacia by castration, favor the theory that the ovary is overactive.

The subject is further complicated by the discovery that at least some of the ductless glands of the fœtus probably functionate *in utero.* Carlson[97] has shown that pregnant pancreëctomized bitches survive longer; Bell,[14] that thyroidectomized bitches are less affected when pregnant, and Halstead[98] that the young of these animals have enormous thyroids. Werelius,[99] however, concludes that the fœtal parathyroids are inactive, as parathyroidectomized animals die sooner than non-pregnant ones (?). Evidently not all the glands functionate.

In view of this uncertainty, no attempt to classify conditions in pregnancy into hyperfunctional and hypofunctional can be made.

B. *Physiological Variations*

The changes in the general organs will be found in Hofbauer's article.[100] Erdheim and Stumme [101] describe the anatomical alterations of the hypophysis. Bone changes (osteophytes, Rokitansky;[102] pelvic joint changes, Loeschke[103]), increase in height in youthful pregnant women, coarsening of the

[90] Sehrt, E. München. med. Wchnscht., 1914, lxi, 293.

[91] It is a well-known fact that the ovaries in fibroids are large and contain numerous follicles. Seitz (München. med. Wchnschr., 1911, lviii, 128) believes that increased or altered ovarian secretion causes the fibroid growth and hence X-ray of the ovaries has a curative effect on the fibroids.

[92] Lane-Claypon, J. E., and Starling, E. H. Proc. Roy. Soc. Med., 1906, lxxvii, Series B, 505.

[93] Schickele, G. Arch. f. Gynäk., 1912, xcvii, 409.

[94] Fellner, O. O. Arch. f. Gynäk., 1913, c, 641.

[95] Even the decidua has had an internal secretory effect ascribed to it (see Gentili, reviewed J. Am. M. Ass., 1913, lxi, 2086).

[96] Seitz, L. Innere Sekretion und Schwangerschaft, 1913.

[97] Carlson, A. J., and Drennan, F. M. Am. J. Physiol., 1911, xxviii, 391.

[98] Halstead, W. S. Johns Hopkins Hosp. Rep., 1896, i, 373.

[99] Werelius, A. Surg., Gynec. & Obst., 1913, xvi, 141.

[100] Hofbauer. Die Graviditätsveränderungen der Organe in klinischer Beleuchtung. Samml. klin. Vorträge, Gyn. No. 210.

[101] Erdheim, J., and Stumme, E. Ziegler's Beitr., 1909, xlvi, 1.

[102] Rokitansky. Lehrbuch der pathologische Anatomie, 1861.

[103] Loeschke, H. Arch. f. Gynäk., 1906, xcvi, 525.

features and extremities (even to recurrent acromegalic symptoms in succeeding pregnancies [Marek[104]]), are ascribable to stimulation of the hypophysis. The frequent hypertrichosis (Jellinghaus[105]), pigmentation lipoidæmia and cholesterinæmia[106] and decreased sugar tolerance may all be accounted for by the noticeable increase of the fascicular and reticular layer of the adrenal (Kolde[107]). The thyroid enlarges in 65 to 90 per cent of all pregnancies (Ward,[108] Seitz[96]).

The hyperplasia of the breast has been variously ascribed to the effect of the fœtus, placenta, and corpus luteum (Halban,[87] Starling,[92] Biedl and Königstein,[109] Frank and Unger,[62] Aschner and Gregoriu,[110] etc.). The evidence is conflicting. When the breast development has once set in, removal of the ovaries does not affect its continuance, and when the products of conception are removed (with or without the removal of the uterus and ovaries), milk secretion occurs.

C. *Pathological Variations*

a. Three diseases, of which one is always associated with pregnancy, the others most frequently occurring during gestation — eclampsia, osteomalacia, and tetany — have been ascribed to derangement in function of the ductless glands.

Eclampsia. No proof warranting discussion has been adduced. A short review of the supposed etiology will be found in my recent paper.[111]

Osteomalacia. The fact that 87 per cent of pregnancy osteomalacia (with or without emptying of the uterus) and 93 per cent of puerperal osteomalacia is cured by double oöphorectomy (Seitz[96]) favors the view that the ovaries are overactive. As adrenalin injections (Bossi[112]) ameliorate or cure some cases (20 per cent, Seitz,[96]), it has been held that the ovarian hyperfunction inhibits adrenal action (Cristofolleti[113, 114, 115]).

Tetany. During pregnancy, as also in tetany occurring at other times, the parathyroids are found hypertrophied. The exact explanation (there may be an increased need for parathyroid secretion [?] — deducible from the fact that partially parathyroidectomized animals develop tetany during pregnancy) is still lacking. The greater nerve irritability, physiological in pregnancy, has also been ascribed to deficiency of the parathyroids.

b. *Thyroid.* Disturbances of the thyroid (Graves' disease, struma) and of the pancreas (diabetes) are usually increased during pregnancy.

c. *Adrenal insufficiency* (Addison's disease) usually produces sterility. In the four recorded cases of pregnancy no abnormalities occurred (Novak[116]).

Several observations of puerperal uterine inversion (Mansfeld[117]) in which the adrenals were found hypoplastic have been regarded as pointing to a connection between these conditions. The frequent occurrence of gall-stone attacks in the puerperium has been ascribed to the lipoidæmia and cholesteræmia of pregnancy (McNee[106]).

Habitual abortion in the early months, when mechanical causes, syphilis, etc., can be excluded, has recently been ascribed to deficient or defective corpus luteum development (R. Meyer[31]). That double oöphorectomy, after the first few weeks, need not disturb pregnancy[58] makes this hypothesis unlikely.

These few and disconnected observations

[104] Marek, R. Zentralbl. f. Gynäk., 1911, xxxv, 1612.
Nolen, W. Berl. klin. Wchnschr., 1909, xlvi, 2177 and 2244.

[105] Jellinghaus, F. Bull. Lying-In Hosp., 1909, v., 212.

[106] During pregnancy the blood contains an increase in cholesterin ester; this may account for the frequent gall-stone attacks noted post-partum (cholesterin stones — Aschoff).
McNee, J. W. Deutsche med. Wchnschr., 1913, xxxix, 994.

[107] Kolde, W. Arch. f. Gynäk., 1913, xcix, 272.

[108] Ward, G. G. Surg., Gynec. & Obst., 1909, 617, ix.
Goodall, J. R., and Conn, L. C. Surg., Gynec. & Obst., 1911, xii, 457.

[109] Biedel and Königstein. Ztschr. f. exp. Path. u. Therap., 1910, vii, 358.

[110] Aschner, B., and Gregoriu, Ch. Arch. f. Gynäk., 1911, xciv, 766.

[111] Frank, R. T. Am. Med. 1913, xix (N. S. viii), 482.
Kownatzki. München. med. Wchnschr., 1910, lvii, 1549.

[112] Bossi, L. M. Zentralbl. f. Gynäk., 1907, xxxi, 69 and 172.

[113] Cristofolleti. Gynäk. Rundschau, 1911, v, 113 and 169.

[114] Novak, E. Zentralbl. f. Gynäk., 1913, xxxvii, 1564; finds no evidence of bone changes in adrenalectomized rats.

[115] McCrudden (McCrudden, F. H. Arch. Internal Med., 1910, v, 596; McCrudden and Fales, H. Ibidem, 1912, ix, 273; McCrudden. Deutsche Arch. f. klin. Med., 1913, cx, 90) has performed careful studies on metabolism in puerperal and non-puerperal osteomalacia and in bone diseases. He comes to the conclusion that oöphorectomy cures puerperal osteomalacia, by preventing further pregnancies. The diseases are due to a continued overexcretion of calcium through the fæces, but what causes this undue drain is not certain.
Very possible disturbance of interrelation (parathyroid?) is at fault, and perhaps adrenalin injections may thus, in certain cases, have restored equilibrium (R. T. F.)

[116] Novak, E. Arch. f. Gynäk., 1913, ci, 36.

[117] Mansfeld, O. Zentralbl. f. Gynäk., 1913, xxxvii, 843.

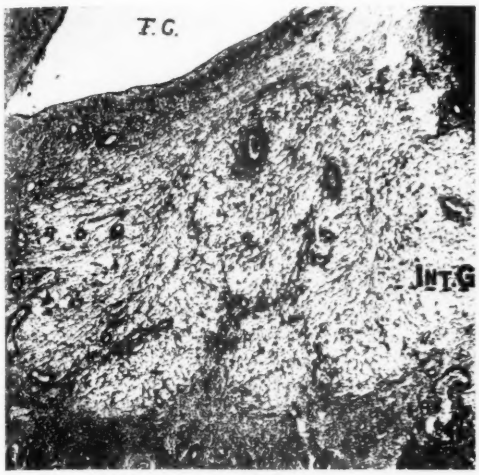


Fig. 1. Interstitial gland, low power. Above, the follicular cavity of an atretic follicle is shown; its lower margin forms the interstitial gland. F. C., follicle cavity.

include the main facts known concerning the changes in pregnancy.

VIII. Diagnosis

The complex mechanism, which produces the various functional disturbances discussed in this paper, can never be solved by the routine gynecological examinations as now practiced. In order to attain progress, much clinical research is necessary. The outline here given contains suggestions, which will vary in each case and which will undoubtedly require modification as new facts are elicited. In a modern hospital the coöperation of the various staffs (gynecological, obstetrical, röntgenological, pathological, chemical, etc.) can be enlisted to make the task of each individual less arduous.

A. *Local examination, including* —

a. Internal genitals: Size and position of uterus, relation of cervix to fundus, shape of vagina and fornices; examination of curettings (with regard to menstrual phase); study of removed ovaries and uteri.

b. External genitals: Development; especially of clitoris.

c. Type of pelvis: Infantile, feminine, neuter; measurements.

Fig. 2. Interstitial gland, high power. A portion of Fig. 1 with higher magnification.

B. *General examination, including* —

a. Secondary sex characters: Hair distribution (mons, perineum, axillæ, face, etc.); fat distribution (especially on nates, lower abdomen, supraclavicular fossæ, supra-orbital); larynx and voice; dimensions (length, relation of extremities to trunk); breasts (size, shape, fat or gland, nipples).

b. Size of thyroid (also pulse rate, tremor, eye symptoms); acetonitrile test of Reid Hunt.[118]

c. Enlargement of lymph-nodes; thymus persistence if ascertainable.

d. X-ray of sella turcica if acromegalic or eunuchoid symptoms are found, also of epiphyses of long bones when dimensional anomalies are encountered. In appropriate

[118] Hunt, Reid. J. Am. M. Ass., 1907, xlix, 240. Mice fed with 1 ccm. of blood from a case of exophthalmic goiter required twice as much acetonitrile (CH_3CN) to kill them (0.70 mgr.) as mice feed on normal blood (0.38 — 0.39 mgr. acentonitrile).

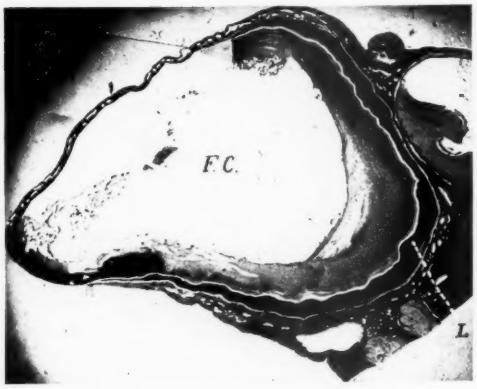


Fig. 3. Cross section of ovary; corpus luteum in stage of vascularization. F. C., follicle cavity; L., lutein cells. Slightly retouched to show distribution and width of lutein layer.

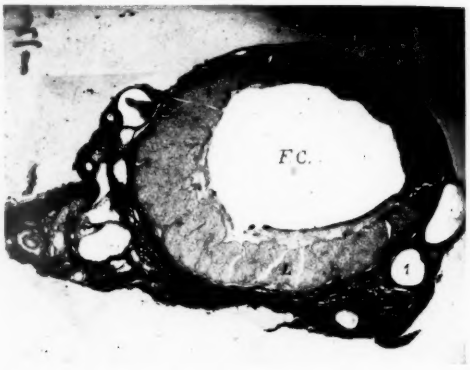


Fig. 4. Cross section of ovary; corpus luteum in stage of ripeness. 1, One of several large atretic follicles. Shows thick, crenated lutein layer. F. C., follicle cavity; L., lutein cells.

cases the ocular fundi, the field of vision (sight, color); reaction of nerves to electricity must be tested.

C. *Blood examination*

a. Full blood count (number of leucocytes, proportion of neutrophiles, lymphocytes, and eosinophiles are most important [Dirks[119]]).

b. Coagulation time (by Wright's method or some modification [A. Keller[120]]).

c. Blood-pressure.

d. In appropriate cases investigations of the amount of glycogen, lipoids (fat, cholesterin, and cholesterin esters).

[119] Dirks, M. Arch. f. Gynäk., 1912, xcvii, 583.
[120] Keller, A. Arch. f. Gynäk., 1912, xcvii, 540.

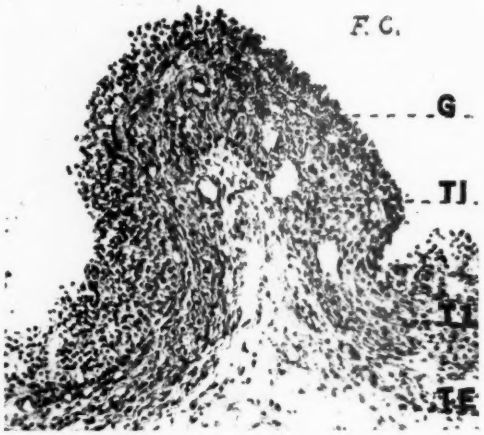


Fig. 5. Recently ruptured follicle. This, as are most of the succeeding microphotographs, is a section from the wall. The follicle cavity (F. C.) is empty; the margin of the granulosa (G), or epithelial lining, is feathery; the cells retain their appearance and distribution as in the unruptured follicle. The theca interna cells (T. I.) are relatively large and numerous. The theca externa (T. E.) is fibrillar.

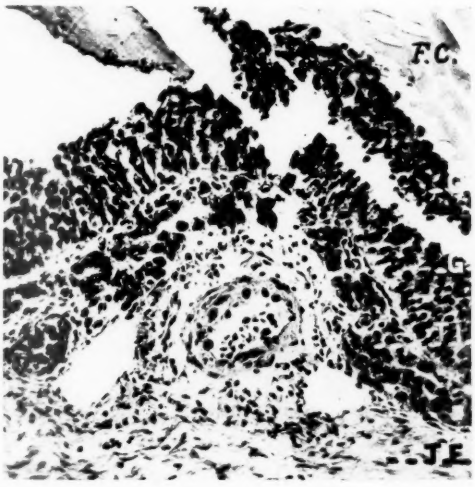


Fig. 6. Corpus luteum; early proliferative stage. The follicle cavity (F. C.) contains coagulated serum. The granulosa cells have increased in number. The theca lutein cells are prominent.

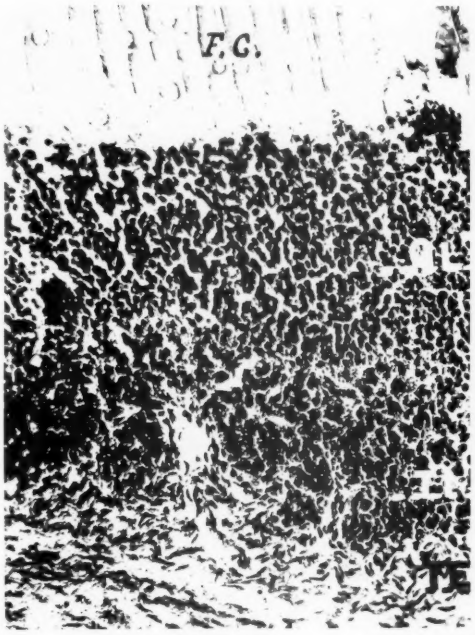


Fig. 7. Corpus luteum; later stage of proliferation. The granulosa cells (G. L.) have multiplied. They still show distribution as in the follicle and contain no lutein.

Fig. 8. Corpus luteum; early vascularization. The follicle cavity contains red blood-cells. The granulosa cells have become lutein cells (L). Numerous, fine, irregularly distributed blood-vessels have penetrated between the lutein cells. The theca lutein cells are unusually numerous in this specimen.

D. *Sugar tolerance* (increase, decrease, amount of dextrose necessary to produce glycosuria [Stolper,[81] R. Keller[121]]).

E. *Reaction to drugs, especially to* —

a. Adrenalin (local mydriatic, general glycosuric).

b. Pilocarpin (sweats diminished in hypofunction, increased in hyperfunction).

c. Atropin.

F. If the services of a physiological chemical laboratory can be enlisted, metabolism examinations in cases of special interest. These would include —

a. The respiratory coefficient (relation of O_2 intake to CO_2 excretion).

b. Analysis of the food intake (fat, protein, carbohydrate, P_2O_5 S, Ca, Mg, etc.).

c. Simultaneously similar analysis of the urinary and fæcal excretion, and of the intermediate products of metabolism.

The numerous current reports based solely upon the urinary excretion are of no value, as in many diseases deficient or increased excretion through the kidneys is compensated by an increase or decrease of excretion through the bowel. A careful record of even a limited number of cases observed with regard to the factors just indicated would prove of far greater value than large numbers of incomplete reports in which one or more isolated phenomena are studied. The value of such clinical research, which is urgently needed, would be further enhanced by extending the observations to three periods—before, during, and after treatment.

[121] KELLER, R. München. med. Wchnschr., 1913, lx, 2162.

Fig. 9. Corpus luteum; end of vascularization. The follicle cavity has been invaded by spindle-cells which begin to shut off the central clot from the lutein layer. The radial distribution of the blood-vessels is complete. The theca lutein cells form a narrow marginal layer. The theca externa (T. E.) is increasingly vascular.

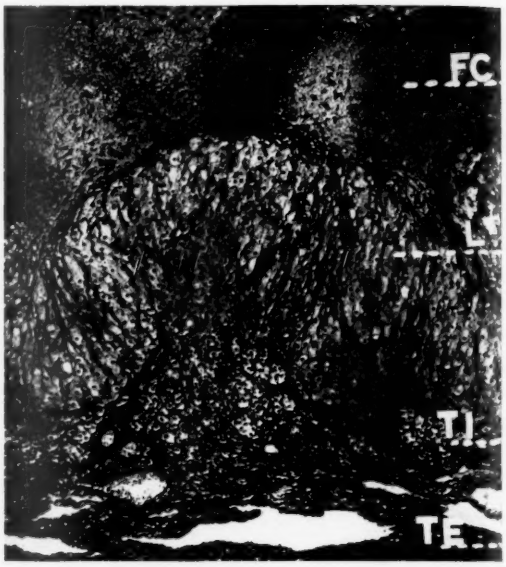


Fig. 10. Corpus luteum. Stage of ripeness (early). The central clot is well shut off. The crenated margin is defined. The radial vessels are numerous.

IX. Treatment

With the exception of the application of the X-ray, a few pioneer attempts to transplant and to resect portions of the ovary and corpora lutea, and the tentative use of some new organ extracts (anterior lobe of the hypophysis, pituitrin, adrenalin), few changes can be recorded in the last three years.

1. *Organotherapy.* In the main this method of treatment has proved disappointing. Thyroid extract is the only substance which has shown the full physiological effect of the gland (probably because the active principles are stored in the gland — "*Vorratsdrüse*" — instead of passing into the circulation almost as rapidly as formed).

a. *Ovotherapy.* Various forms of the extract of the entire ovary and of the corpus luteum have been tried. My own views have undergone but little modification since 1910.[122] Favorable reports continue to appear in the literature concerning the oral administration of ovarin, oöphorin, ovario-lecithin-yohimbin, lutein, etc., and subcutaneous use of ovarin (Poehl), lutein, etc. The chief effect noted appears to be relief of the vasomotor symptoms. Recently Adler [83] has reported that after administration of ovarin by mouth, in two cases of amenorrhœa, he was able to demonstrate premenstrual and menstrual changes in the uterine mucosa. A similar result in castrates would prove more convincing.

Recent experimental reports dealing with the use of *lipoid extracts of the ovary and placenta* appear to show a specific stimulating effect on the uterus (Iscovesco,[123] Fellner,[124] Adler,[125] Herrmann[126]). The most complete report, that of Fellner, indicates that these extracts are extremely toxic. Schickele[127]

[122] Frank, R. T. Arch. Internal Med., 1910, vi, 314.
[123] Iscovesco, H. Compt. rend. de l'Acad., de Sc., 1912, clv, 1104.
[124] Fellner, O. O. Arch. f. Gynäk., 1913, c, 641.
[125] Adler, B. Arch. f. Gynäk., 1913, ci, 534.
[126] Herrmann, E. Zentralbl. f. Gynäk., 1913, xxvii, 1563.
[127] Schickele. Ztschr. f. d. ges. exp. Med., 1913, i, 539.

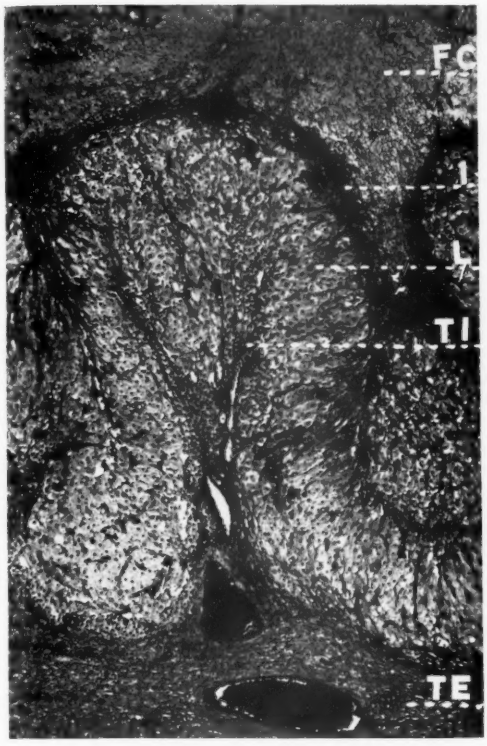


Fig. 11. Corpus luteum. Stage of ripeness (late). The characteristics mentioned under Fig. 10 are accentuated, particularly the walling-off of the central clot (1). Theca lutein cells are noted only in the septa.

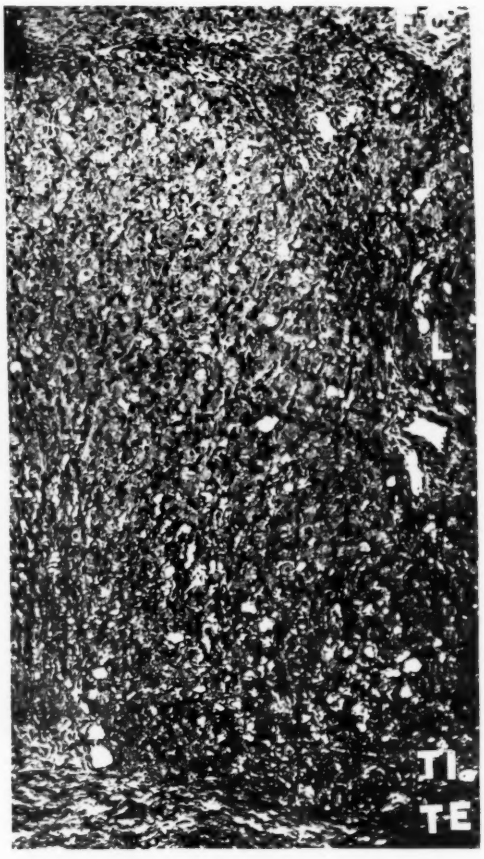


Fig. 12. Corpus luteum; stage of regression. The follicle cavity contains firm connective tissue replacing the clot. The lutein cells are irregular in size. Many have fallen out leaving gaps.

has used ovarian extract (without corpus luteum) prepared by subjecting the tissue to high pressure in a Büchner press. This phase of the question is still in its infancy.

From the foregoing reports it appears justifiable, when so disposed, to exhibit ovarian extracts in hypofunctional conditions of the genitals. The administration by mouth is harmless; subcutaneous introduction requires caution.

b. *Thyroid extracts.* Even this physiologically active extract has given variable results. Personally, I have obtained fair results in amenorrhœas complicated by obesity, if the genital atrophy was not extreme and the thyroid gland appeared diminished in size. In some cases in whom five grains, twice daily, did not produce tachycardia, menstruation was reëstablished in from four to eight weeks. The obesity did not diminish. Striking results were obtained with small doses (one gr. twice daily) in the early months of pregnancy, for the relief of nausea and vomiting.[128] Unless the symptoms improve within two to three days, and no tachycardia is noted, the treatment regularly fails.

Sehrt has just reported[90] the successful use of iodothyrin in functional menorrhagias. He warns that success is met with only in cases in which the coagulation time of the blood is decreased, and that

[128] Siegmund, A. Zentralbl. f. Gynäk., 1910, xxxiv, 1349; uses larger doses, from 2 to 12 grains of thyroidin.

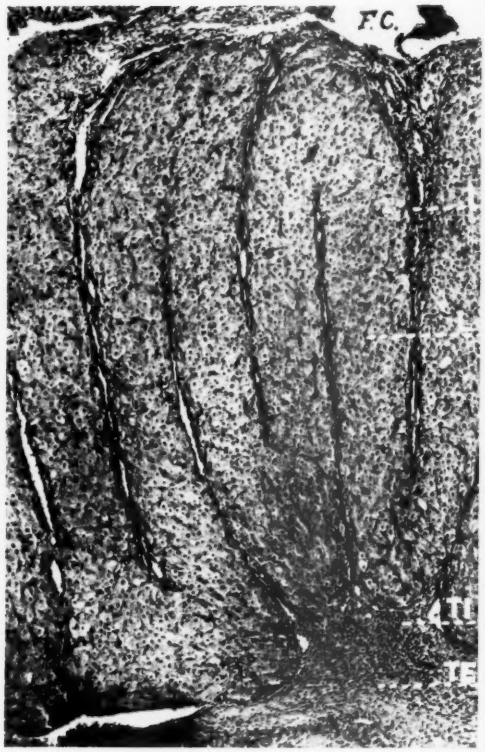


Fig. 13. Corpus luteum of pregnancy (second month). Note resemblance to cortex of adrenal. The septa (1) are well-defined and regular.

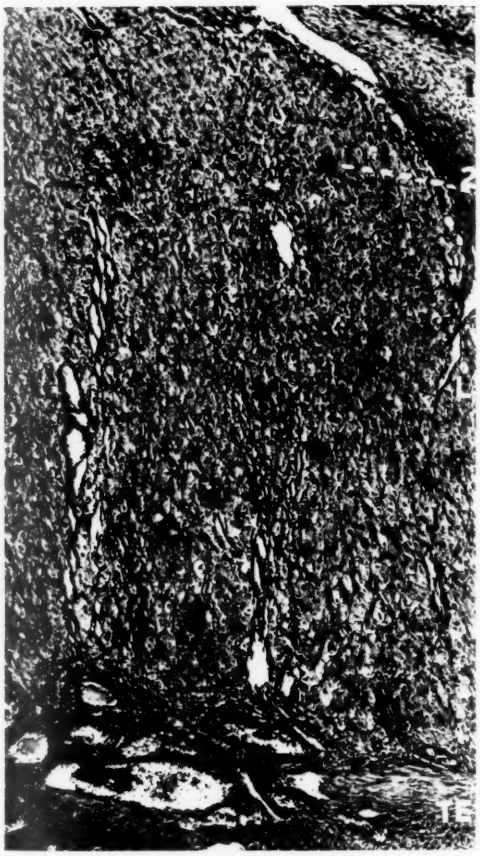


Fig. 14. Corpus luteum of pregnancy (fifth month). (1) shows firm fibrous core replacing central cavity. (2) areas of calcification. The lutein cells are smaller and less regular than in the earlier months.

throughout the course of the treatment the coagulation time must be rigidly controlled by frequent tests. (Lehmann[129] reports success from the use of potassium iodide in habitual abortion, the iodide acting as a stimulant of the thyroid gland.)

c. *Adrenalin* does not contain the entire physiological properties of the adrenal gland. Recently a lipoid, as yet not studied, has been isolated from the cortex.[130] Adrenalin has been employed with success for osteomalacia (*vide ante*) by Bossi [112] and others.

d. *Pituitary extracts.* Anterior lobe extracts have been recommended for the adipose type of genital atrophy (Cushing). *Pituitrin*, extract of the posterior lobe, is valuable mainly as a stimulant of contraction in labor. Its use is now too well known to require mention. In two cases, in one of which the cervix was completely dilated, alarming tetanus uteri developed after the use of but one cubic centimeter, necessitating the employment of deep narcosis. The pituitrin effect on the uterus must be regarded as purely local and in the nature of a simple drug action (stimulation of the nervous pelvicus [131]).

e. *Thymus and pineal extracts* are marketed. As yet no trustworthy reports of their effect on the genitals has appeared.

[129] Lehmann. Arch. f. Gynäk., 1913, ci, 205.

[130] Voegtlin, C., and Macht, D. I. J. Am. M. Ass., 1913, lxi, 2136.

[131] Frankl-Hochwart, L., and Froehlich, A. Arch. f. exp. Pathol. u. Phar. mak., 1910, lxiii, 345.

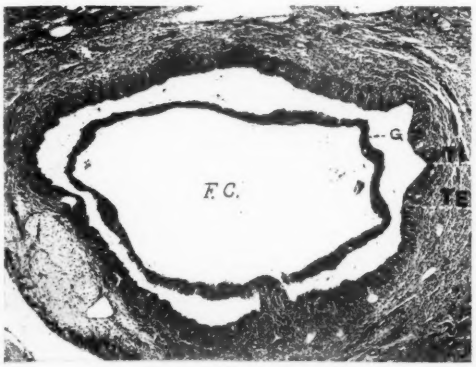


Fig. 15. Transverse section across an atretic follicle. During fixation the epithelial (granulosa [G]) layer has shrunk away from the theca interna, thus plainly showing their relative thickness.

f. *Combined organotherapy* is advocated, especially by French authors. The subject is too obscure to permit of intelligent discussion at the present time.

2. *X-ray treatment of hyperfunctional troubles.* Persistent menorrhagias and metrorrhagias without anatomical basis respond well to the röntgen ray. This method of therapy is a great boon in the functional hæmorrhages of puberty. It has cured extreme cases in which local treatment (repeated curettage), calcium lactate by mouth or rectum, or serum injections had failed, and in which hysterectomy had been advised as a last resort. I have used it with success in adults, and at the time of the climax (invariably excluding malignant disease of the uterine cavity by curettage *before* beginning the treatment). At puberty, considerable doses, given at intervals in order to allow an occasional menstruation to occur, are necessary. When the menses become scant and infrequent the treatment may be stopped, and the patient kept under observation. In patients from 30 to 35 years of age, who do not desire to lose their menses permanently, the exposures should be continued until slight climacteric molimina or amenorrhœa develops. Menstruation, usually approaching the normal, reappears in four to eight months. These patients should be watched for relapses. Older patients readily become permanently amenorrhœic. I am as yet unable to state whether more careful dosage and earlier stoppage of the exposures can prevent the annoying climacteric symptoms which occasionally develop. Whether the röntgen ray produces permanent injury to the ovary and exerts a deleterious effect on pregnancy (fœtus) years after the treatment has been stopped, is not yet determined. This possibility should be kept in mind.

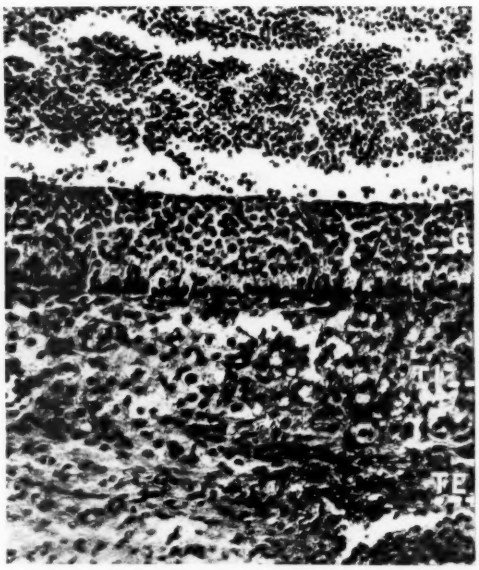


Fig. 16. Wall of atretic follicle. The follicle cavity contains detritus. The margin of the granulosa is smooth. The theca interna is wider than the epithelial layer.

In a few cases of subacute chronic and inflammatory disease of the adnexa, in which operation was either refused or contra-indicated, and in which profuse and repeated hæmorrhages occurred, the X-ray was of use. In these cases rapid effects must be obtained, as the preliminary stage of excitation (and increased bleeding) is pronounced.

The suggestion to utilize this preliminary stage of ovarian stimulation, in cases of hypofunction, does not appeal to me, because it is impossible to graduate the dosage with sufficient accuracy to avoid increasing the ovarian deficiency.

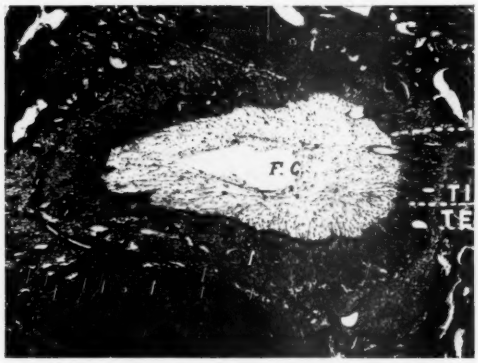


Fig. 17. More advanced atresia. The follicle cavity has been almost completely obliterated by fine connective tissue. The lining epithelium has disappeared. (1) The characteristic hyaline band, external to which are theca lutein cells.

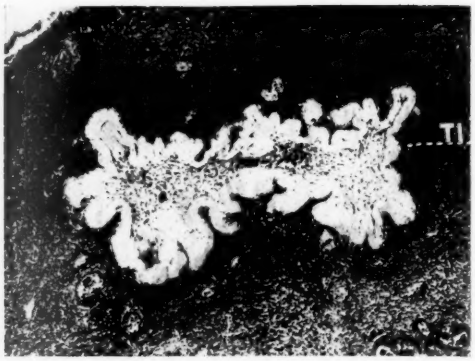


Fig. 18. Advanced atresia. The follicle cavity is completely obliterated. The hyaline band has shrunk and, therefore, assumes bizarre contours. The theca interna cells are resuming their spindle-form, and the outline of the follicle is no longer definable from the ovarian stroma.

3. *Resection of the ovary. Microcystic.* (Dysmenorrhœa, Sterility). Henkel[132] reported relief of dysmenorrhœa and anomalous menstrual bleeding after resection of the ovaries. Reynolds,[74] who suggests that the change is often secondary to mild tubal infections, likewise reports a high percentage of cures.

In the present stage of uncertainty it appears unjustifiable to perform a laparotomy without some stricter indication than dysmenorrhœa or sterility. When encountered incidentally during an abdominal operation, wedge-shaped resection may be performed.

4. *Transplantation of the ovary.* Numerous reports of primarily successful homotransplantations and heterotransplantations (Martin[133]) are on record. The consensus of opinion is that the operation does not give permanent results. The implanted ovaries eventually become absorbed, after the follicle apparatus has undergone cystic degeneration and destruction. To avoid the necessity of extensive secondary operations, in such cases in which disturbing symptoms arise from the transplants, it is advisable to place the grafts in well-vascularized but accessible regions (the rectus abdominis).

5. *Local uterine treatment.* With the advance in our knowledge the uselessness of indiscriminate curettage has become apparent. In sterility it is of no value. In hyperplastic menorrhagias (fungoid endometrium), occasionally permanent, more often only transitory, relief is obtained. In this type, however, curettage retains its importance as a diagnostic agent (to differentiate from neoplastic processes).

The stem pessary used in infantilistic genitals may produce an accentuation of the decidual reaction (*vide ante*). At present it is employed empirically. The various plastic operations on the cervix devised for sterility and dysmenorrhœa act mechanically (drainage, etc.) and, therefore, do not enter into this discussion.

The nasal treatment of dysmenorrhœa[134] probably causes improvement through the nervous system; a recent research by Koblanck and Roeder[135] showed hypoplasia of the genitals developing in animals, after resection of the turbinates.

6. *General systemic treatment.* As our means of affecting the genital organs by specific drugs are still unsatisfactory, general measures have not lost their value as therapeutic agents. If employed near adolescence, general hygienic measures (exercise, fresh air, proper clothing, diet, hydrotherapy, tonics, etc.) may assist either in curing, or at least arresting, the advance of hypofunctional

[132] Henkel. München. med. Wchnschr., 1911, lviii, 337.
[133] Martin, F. H. Surg., Gynec. & Obst., 1908, vii, 7.
[134] Brettauer, J. Surg., Gynec. & Obst., 1913, xvii, 381.
[135] Koblanck and Roeder, H. Berl. klin. Wchnschr., 1912, xlix, 1893.

troubles such as amenorrhœa, dysmenorrhœa, and sterility. In the true obesities (as distinguished from "*Mastfettsucht*") restriction of diet is of minor value. Improvement in general health, at all periods of life, helps to ameliorate the many concomitant nervous phenomena, which so frequently form the chief complaints of gynecological patients.

7. *Drug treatment.* For the sake of completeness drug treatment must be mentioned. It is of little value. In dysmenorrhœa, Drenkhan [136] has recommended atropine (injections into the cervical tissues, locally applied by means of tampons or by mouth). Adler [125] believes that it acts only on vagotonic individuals. For the pain, narcotics are frequently necessary. The use of drugs which are supposed to stimulate the pelvic organs, such as aloes, yohimbin, etc., is illusory. Functional menorrhagias and metrorrhagias fail to respond to ergot, hydrastis, styptol, etc.

X. General Summary

In this paper the attempt has been made to emphasize the following facts:

1. That the glands of internal secretion control and regulate many vital processes, including development, growth, nervous impulses, psychical manifestation, metabolism, and reproduction.

2. That each gland, regarded individually, exerts a predominant influence upon one or more of these functions.

3. That in order to produce a perfect individual and maintain perfect health, the interaction of these glands must be normal.

4. That disturbance of this perfect interrelation reacts upon the genital sphere in only one of two ways — in an increase or a decrease of function.

5. That the gonads, in turn, may react on one or more of the other ductless glands, causing a multitude of variations.

6. That the ovary, through which all impulses to the genital tract are transmitted, or in which they originate, is a compound organ (like the hypophysis or adrenal) made up of at least two (follicle apparatus, corpus luteum) or perhaps three (interstitial gland) components.

7. That of these components, the follicle apparatus (and perhaps the interstitial gland) controls the growth and nutrition of the genitals, the corpus luteum controlling the periodicity and production of the cyclical changes.

8. That the local pregnancy changes are probably accounted for by the persistence of the corpus luteum, but that the products of conception, which surely cause the persistence of the yellow body, may share in causing both the local and systemic phenomena accompanying pregnancy.

9. That genital hypofunction manifests itself clinically chiefly as follows:

a. Anatomically: locally, by aplasia of the genitals; systemically, by the signs of infantilism, eunuchoidism, and other variations depending upon the time of onset and the other ductless glands most affected.

b. Symptomatically: by scant or infrequent menstruation, amenorrhœa, dysmenorrhœa, and sterility.

10. The genital hyperfunction manifests itself clinically chiefly as follows:

a. Anatomically: locally, no change, "metritic type," fibroids (?); systemically, often no change.

b. Symptomatically by too profuse, too prolonged, or too frequent menstruation; occasionally, by overfertility.

11. That our present methods of diagnosis require extension and refinement.

12. That organotherapy is unsatisfactory, X-ray treatment valuable in default of better, resection and transplantation of the ovary purely tentative, local treatment nearly powerless, and general hygienic measures still our mainstay.

13. Finally, that further progress will depend upon intensive study of anatomical material in connection with elaborated functional diagnosis and symptomatology, instead of upon haphazard empiric therapy.

[136] Drenkhan. Zentralbl. f. Gynäk., 1910, xxxiv, 1531.

VOLVULUS: TORSION OF THE WHOLE MESENTERY

Report of Case with Résumé of the Literature

By RALPH E. WEIBLE, M. D., Fargo, North Dakota

CASE HISTORY: Ira H., 27 years old, a well-built man weighing 150 pounds, says that he has had some kind of abdominal trouble as long as he can remember. He recalls that as a small boy he had sharp attacks of colic. He has been bloated at times and has been constipated all his life. With the aid of laxatives his bowels have moved three or four times a week. At eighteen he stopped taking physic, since which, after three days of constipation, towards evening he would have a sharp pain in the right lumbar region extending as high as the clavicle. This would last half an hour and would be followed by a bowel movement. This cycle of symptoms would again appear three days later. He further states that a heavy meal would be followed by an epigastric distress extending around the right side to the axillary line.

Previous to his recent illness he drove a traction engine for a week. There was a constant jarring from this and his posture upon the machine was a peculiar one. He rested his right knee upon the tool-box and carried the weight of his body on the other leg. The following Monday he drove a wagon ten miles. Tuesday he lifted a heavy stove. Wednesday morning at 3 A. M. he was awakened by a severe pain which extended across the abdomen. At 7 A. M. morphia was given. Pulse and temperature were normal, and he passed gas. Thursday and Thursday night his condition was worse; the colicky pain extending clear across the abdomen was continuous and showed no localization. He vomited many times and had a diarrhœa which was ascribed to physic that had been given him. By Friday the diarrhœa had ceased and an enema gave no result. Four or five times he vomited a dark liquid. The pain remained the same, but a hypodermic of morphia at noon gave some relief. Accompanied by his physician, he came to the hospital that evening.

Examination showed a man who looked sick and who complained of pain over the whole abdomen. There was moderate tympanites and tenderness to pressure everywhere. No peristaltic wave was to be seen, though perhaps this was due to morphia administered before taking the train. There was no local enlargement or induration; in short, there was no focal sign of any kind; instead, muscular rigidity was evenly distributed. Temperature, 100°; pulse, 84; respiration, 20.

The onset, pain, and vomiting suggested an ileus. The early passage of gas and the loose bowel movements of the previous day seemed to negative it. Though a diagnosis was impossible, a menacing condition was plainly present. Operation was immediately performed.

Operation, May 23, 1913: An incision was made at the outer edge of the right rectus, and was doubled in length on noting the condition of the presenting coils. All of the small intestine was badly distended, was dark red in color, and turned to blue on manipulation. Serum was present in only moderate amount. A careful search for the cæcum failed, but proved it was absent from the right side. Examination of the root of the mesentery cleared up the mystery — the whole mesentery was twisted so tightly that it felt like an inch rope. The torsion was a little more than 180° in the direction of the hands of the clock. When the whole of the small intestine was eviscerated, the cæcum was pulled into view from the left lumbar region. There was a common ileocæcal mesentery. The mesentery to a point on the ileum a few centimeters from its end seemed far too short, and exerted so much traction as to obstruct the bowel. Proximally, the ileum was badly distended; the few centimeters distal and the ascending colon were only moderately distended. (Later on your attention will be again called to these mesenteric folds.) The twisting was reversed and the intestines returned within the abdomen. With the slightest coaxing, gas freely passed from the badly distended small bowel into the cæcum. A small drainage tube was placed into the pelvis and the wound closed.

The patient was returned to bed in good condition, placed in the Fowler position, and saline by the Murphy method begun. Recovery was uneventful. There was no post-operative vomiting, and gas passed the following noon; by evening this was accompanied by colored water, and the next evening a Noble's enema was followed by a bowel movement which gave great relief. He left the hospital on the nineteenth day and has remained well.

A careful review of the literature showed but two successful cases in America: that of Shepherd in Canada, reported in 1898, and George Tully Vaughan's case in our own country, reported in 1907. This is sufficient reason for discussing the subject.

To determine and select the cases has been a matter of great difficulty, since the main facts are given but by few, and many of the reports are so incomplete that the extent of the volvulus cannot be determined. Whatever else is omitted, the phrase "torsion of the whole mesentery" should appear with

every report. Most attempts at collecting have been made within the bounds of certain languages. Fantino states that but 14 cases, including the unsuccessful ones, had been reported up to 1906. Lerda, quoted in Burghard's System of Surgery, says that up to 1908 only five cases, including his own, had been successfully operated upon. The following list of recoveries seems to be genuine and proves that these statements are too conservative.

1892 Brown, Maj. W. R. (probable).
1898 Shepherd, F. J. (quoted by Vaughan).
1901 Williams, Maj. C. L. (probable).
1904 Whiting.
1905 Philipowicz, two cases.
1905 Möhring (quoted by Danielson).
1907 Hutchinson, Jonathon.
1907 Bull, P.
1907 Tesson, René.
1907 Schultze.
1907 Vaughan, Geo. Tully.
1908 Lerda, G.
1909 Costa (quoted by Fantino).
1909 Blecher.
1909 Brunswic Le Bihan.
1909 Billington.
1910 Wille, two cases.
1911 Fantino.
1911 Newton, H. A. S.
1912 Bosquette.
Twenty-two cases.

A further compilation of 45 cases, some unsuccessful, some post-mortem findings, has been secured and has been consulted whenever there is a variety of opinion among the observers.

Most often the age is given as "after middle age" or "among the old." Where it could be ascertained it was found to be —

Up to 10 years	10 cases
Up to 20 years	7 cases
Up to 30 years	13 cases
Up to 40 years	4 cases
Up to 50 years	8 cases
Up to 60 years	10 cases
After 60 years	8 cases

Moreover, it has often occurred within the first ten days of infant life — the volvulus of the new-born. It can be seen, then, that it occurs at all ages, but with the fewest cases between 30 and 40.

The male sex is peculiarly disposed. In 64 cases, 13 were women and 51 men. No reason for this selection has been advanced.

As to the direction of the twist, by far the majority indicated it by the phrase "from left to right" or "to the left." This is capable of misinterpretation. To carry conviction is to say "in the direction with the hands of the clock," or *vice versa*. Philipowicz, who has had a remarkable experience with volvulus of varying extent, found it in the direction opposite to the hands of the clock in but 2 out of 24 cases. In my list it was opposite to the hands in 7 out of 37 cases.

The anatomy is very interesting: the root of the normal mesentery is about six inches broad, extending obliquely from the left side of the second lumbar vertebra to the right sacro-iliac symphysis, and contains within it the blood-vessels and nerves from the beginning of the jejunum to the cæcum. In these cases it is not so broad and may be more horizontal, and frequently it is longer than usual from the spinous attachment to the gut margin.

In the third fœtal month the duodenum has a mesentery, and the third portion is not the closely attached organ that it later becomes. The colon, too, has not become fixed by a blending of its peritoneal coats to the posterior wall, and the mesentery of the small bowel is continuous with that of the cæcum. P. Michaelis[1] says that this condition persists into the fourth fœtal month. All of the cases in the new-born show this embryonic condition, and, where it was looked for, most authors remark it present in the adult. For this reason, it is a common thing, then, to find a part of the large intestine in the volvulus — the cæcum and even as much as the greater part of the transverse colon. In such cases the cæcum is found near the spleen, or a little lower.

In 1902, Burgess reported the case of an 8-year-old boy who died without operation. His autopsy report is so typical of these cases that it is well to include it. He says: "The small intestine, cæcum, and colon possessed a common mesentery which, while of considerable depth as measured from its spinal to its enteric attachment, was of very limited vertical extent. The root of the common

[1] Wien. klin. Rundschau, 1913, Sept. 21.

	Sex and Age	History	Direction and Degree	Intestine	Result
Fantino	F. 15	No vomiting; sick 5 days; temperature normal; pulse 90.	180, watch	S. I.	Recovered
Fantino	M. 60	Onset sudden; fæcal vomit, great distention eighth day; pulse 110	180, watch	S. I.	Died
Fantino	– 55	Onset sudden; vomiting; much distention third day; pulse 90; temperature normal	180, watch	S. I.	Died
Fantino	M. 52	Onset sudden; vomiting; distention; pulse 80; 24 hours	180, watch	S. I.	Died
Fantino	M. 60	Onset sudden; fæcal vomiting; pulse 100; fifth day	180, watch	S. I.	Died
Rokitansky	F. 71	Following reduction strangulated hernia; death 10 days	720, twist 1½ in. diameter	S. I.	Died
Rokitansky	F. 72	No history. Post-mortem examination: long mesentery	540	S. I.	Died
Rokitansky	F. 72	Post-mortem examination: long mesentery		S. I.	Died
Rokitansky	F. 71	Femoral hernia for 12 years; twist 1½ inches thick, found at post-mortem		S. I.	Died
Brunswic Le Bihan	M. —	Sixth day		S. I.	Recovered
Philipowicz	M. 50	Sick 3 days	360, watch	S. I.	Recovered
Philipowicz	M. 56	Sick 2 days		S. I.	Died
Philipowicz	M. 63	Sick 5 days	360	S. I.	Died
Philipowicz	M. 45	Sick 2 days			Recovered
Eschbach	M. 8 days.	No operation; post-mortem findings: small intestine and transverse colon	Watch		Died; no operation
Hübner	M. 3	Death after extirpation mesenteric cyst; common ileocæcal mesentery		S. I. and ½ colon	Died
Lerda	M. 55	Habitually constipated with occasional attacks of 2 to 3 days' diarrhœa. Sick 6 days; pain, not severe, in sacrolumbar region radiating into front	280, right to left		Died
Homans	F. 7	Sick 5 days; band felt in left inguinal region; hard mass by rectum	Left to right		Died, 24 hours
Lerda	M. 11	Sick 2 days	Watch	S. I.	Recovered
Maj. Debrie	M. young	Sick 48 hours; pulse 106; temperature subnormal. Did not find volvulus at operation. Fold to lower end of ileum and obstructing it. Classical symptoms	Left to right	S. I.	Died
Morestin	M. 44	Taken sick 1 day before; temperature normal, pulse 110. Entire mesentery. Good example of deadliness of some cases	Left to right	S. I.	Died 6 hours after operation
Maj. Williams	M. 30	Sick 21 hours. Boggy mass felt per rectum; entire mesentery	Left to right, 180	S. I.	Recovered
Delore	M. 58	Sick 4 days; fæcal vomit. At operation found obstructing bands; severed; did not find volvulus nor correct same	720, watch		Died next day; bowels gangrenous
Küster	M. 50				Died
Mignon	M. 28	Vomiting; severe pain; frequent desire to stool. Collapse in 24 hours; pulse 150; temperature 99°, death in 41 hours. At operation the twist was 1 inch thick	Left to right	S. I.	Died 5 hours after operation
Maj. Brown	M. 50	Pain; tympanites; intestinal vessels much congested; sick nearly a week.	Left to right	S. I.	Recovered
Monod	F. 15	Pain; obstipation; tympanites; no vomiting; sick 6 days; temperature subnormal; pulse rapid	Left to right	Nearly all S. I.	Died 24 hours after operation
Regnier	F. 50	Distention; tympanites; vomiting; sick 7 days. Intestines gangrenous	Right to left	S. I.	Death
Kirmisson	M. 7	Taken sick March 2; improved. Relapsed March 10; fæcal vomit; no tympanites. Operation; twist mistaken for ligament of Treitze and not corrected	360, left to right	S. I., whole mesentery	Died
Shepherd	M. 27	Appendicectomy 2 years before; sick 2 days; vomiting, constipation, pain below navel; temperature 97.5°; pulse 140	Left to right	S. I., whole mesentery	Recovered
Delbet	F. —	Sick 9 days; at operation, found peritoneal folds and condition like retroperitoneal hernia, entero-anastamosis; post-mortem; found a union between the jejunum and end of the ileum	90, watch	Whole S. I.	Died
Delbet	M. 69	Taken sick in morning; operation that evening; pulse 100; temperature subnormal; fold over ileum near its end; beyond ileum stretched between fold and cæcum, immovable, and flat against back	Right to left 1¼ turns	Nearly all of S. I.	Died 11 days after; pneumonia

	Sex and Age	History	Direction and Degree	Intestine	Result
Fertig	M. 30	Began 2 days after operation for mesenteric cysts	720, watch		Died
Stirling[1]	M. 42	Sick 3 days	Double twist	S. I. last few inches of ileum collapsed	Recovered
Schultze	M. 19	Appendicectomy (acute); vomiting continued 11 days later. Second operation; found abscess had caused a fixation	360	S. I.	Recovered
Robinson	M. 49	Operation for strangulated hernia; 6 weeks later, obstruction; 5 days later, operation. Mesentery 12 inches long, 4 inches wide, chronic mesenteritis	360	4/5 of S. I.	Died
Bull	M. 29	First operation, did not find volvulus; found adhesions 48 hours later at second operation. Sick 9 days before first operation	180, watch	S. I., all but last few cms.	Recovered
Burgess	M. 8	Sick 16 hours; no previous history. No operation, but post-mortem findings given, ileocæcal mesentery	360, watch	S. I. and ½ asc. colon	Died
Philipowicz	M. 55	No previous history; sick 4 days	270, left to right; long mesentery	S. I.	Recovered
Philipowicz	M. 67	No previous history; lifted weight; sick 4 days	270, left to right; band 7 cm. above ileocæcal valve	S. I.	Died
Philipowicz	M. 62	Pain and vomiting attacks before. Band 6 cm. above valve; below empty	270, right to left	S. I.	Recovered
Braun[2]	M. 11			S. I.	Died
Riedel[2]	M. 50		180	S. I.	Died
Von Wahl[2]	M. 41				Died
Wille	F. 41	No past history; few adhesions	180	S. I.	Recovered
Wille	F. 24	Constipated always; no other history	180	S. I.	Recovered
Bruhns[2]	M. 24	Three previous attacks; sick 8 days; pulse 88	360, opposite to watch	S. I. and middle transv. colon	Died in 40 minutes
Blecher	M. 21	Frequent attacks; vomiting and colic; root size of finger	180, left to right	S. I. and asc. col. ileocæcal mesentery	Recovered
Blecher	M. 25	No history; common mesentery	360, left to right	S. I. and middle transv. col.	Died in 12 hours
Billington	M. 41	No history; common mesentery	180	S.I. and asc. col	Recovered
Kuttner	F. 55	No history; very long mesentery	360	S. I. and cæcum	Died
Hutchinson	M. 22	Common mesentery		S. I.	Recovered
Bosquette	M. 45	Negative history		S. I.	Recovered
Frolich	M. 3		Left to right	S. I.	Died
Wandel	M. 7	Common mesentery	360		Died; no operation
Wandel	M. 20	Common mesentery	Watch	S.I. and asc. col	Died; no operation
Möhring	F. 72	Common mesentery	180	S. I. and cæcum	Recovered
Hausmann	M. 22	Negative		S. I. and asc. col.	Died
Helmsmüller					Died
Hübner	M. 3			S. I. and part of trans. col.	Died
Von Manteuffel	M. 20	Lifted meal-sack; sick 6 days	90, right to left	Last ⅓ duodenum to ½ asc. col.	Died
Schreiber	M. 9	Attacks constipation and vomiting since birth; common mesentery.	360, left to right	S. I. and ½ asc. col.	Died; no operation
Whiting	M. 34	Had been operated for acute appendix	270, left to right	S. I.	Recovered
Whiting	M. 5		Right to left	S. I.	Died
Vaughan	M. 22			Entire mes.	Recovered
Tesson	M. 27	Operation, appendix, 7 months before. Obstruction, umbilical pain, green emesis; pulse 80; temperature 37.4°	Watch	S. I.	Recovered

[1] Reported by Newton. [2] Quoted by Richter.

mesentery did not reach below the third lumbar vertebra and was directed much more horizontally than normal, leaving the right iliac fossa quite free from any mesenteric attachment."

The literature abounds with references to adhesions, peritoneal folds, mesenteric folds, or contracted bands fastened to the bowel or obstructing it. Much confusion has occurred from their presence, which at times has led to tragic results. Encountering such a condition, Delbet made an anastomosis and only at autopsy found the volvulus with the anastamosis uniting the jejunum and the terminal ileum. What are these folds or bands? No doubt many are true adhesions and should be severed. Philipowicz says that he nearly always found evidences of previous mesenteritis, so that the mesentery is thickened and shortened at times. But these folds can be formed entirely by the volvulus, as illustrated by the case here given. It is possible that they are produced in the following manner: A loop of bowel is fixed, perhaps by adhesions, or the terminal ileum is anchored by the larger colon, or the mesentery at this point is actually shorter than the rest; then, with the winding up of the mesentery as on a windlass, strong traction is exerted upon the fixed portion. The practical point is that in the presence of obstructing mesenteric folds, nothing should be attempted until after examination of the root of the mesentery.

Another point not clearly understood is the amount of torsion required to produce obstruction. It is usually put at $\frac{2}{5}$ or $\frac{3}{5}$ of a circle. Von Manteuffel's case was only 90° and yet was fatal; and Delbet says that in one of his cases it was but little more than $\frac{1}{4}$ of a circle. If a 90° torsion of the mesentery is pulled tight, there is obstruction to the blood-vessels; if a mesenteric fold to the ileum is pulled taut, or the colon compressed by the mesentery of a loop of small gut drawn tight across it, there is obstruction to the fæcal current; therefore, it is probable that the tightness of the twist and the obstruction of the intestinal contents are the important factors rather than the degree of the torsion. The usual extent is 180°, but two cases of even 720° have been reported.

Etiology. The primary predisposing cause is a developmental anomaly, the most important being a shortening of the mesenteric root in the vertical diameter. A long mesentery with a cæcum mobile would greatly increase the tendency.

Other predisposing causes as given by the different observers are:

1. Old scar formation and chronic mesenteritis (Philipowicz, Küttner, Robinson).
2. Former operations (Whiting, Riedel, Hübner, Schultze, Robinson, Shepherd).
3. Hernia (Rokitansky, Vaughan).
4. Fibrous bands (Tesson).
5. Mesenteric cysts (Hübner, Fertig).
6. Habitual constipation and chronic intestinal stasis with traction on mesentery (Bosquette, Delore).

Among the exciting causes given are:

1. Violent peristalsis from heavy catharsis, overeating, excessive fermentation (Wille, Fantino).
2. Heavy lifting (Von Manteuffel, Fantino).
3. Blow on abdomen (Fantino).

From the foregoing one concludes that given a small-sized mesenteric root and a common ileocæcal mesentery, a torsion can occur from exaggerated peristalsis. A hindrance to peristalsis at certain points, as from a stasis or overfilling or adhesions, would increase the violence of the muscular action of the bowel proximal to it. Bodily strain or trauma would further the possibility.

Symptoms. There are numerous cases that, like the one here presented, give a long history of habitual constipation or attacks of pain, perhaps with vomiting (Bruhns, Schreiber, Krojius, Faltin, Philipowicz, Lerda, Blecher). This has occurred often enough to make it of some importance. Frequently, without previous trouble, the patient is taken with sudden excruciating pain which is either referred to the umbilical region or is not easy to locate. (In one of Lerda's cases it was not severe and was located in the sacro-iliac region radiating into the sides.)

Vomiting is almost invariably present. It may be bilious, but later it is a dark-colored watery material. It is seldom if ever fæcal, since the bowel is incapable of emptying itself in either direction. (Vaughan's case had bloody vomiting as soon as the volvulus was corrected.)

Constipation is, or soon becomes, complete. It is accompanied by more or less tympanites and frequently areas of exaggerated peristalsis are seen. High enemas can often be passed, but return giving no relief. Rigidity is universal.

Temperature is either afebrile or but little above normal; frequently it is subnormal. The pulse is but little changed until collapse threatens, when it becomes weak and fast. Many cases have gone to operation with pulses from 80 to 100; in Fantino's five cases the pulse was 90, 110, 90, 80, and 100, respectively, with but one recovery in the series.

Collapse and death may come as early as 16 hours (Burgess) or as late as two weeks. This great variation depends principally on the completeness of the obstruction of the blood supply. The facial expression in the early hours is merely that of suffering; later, the abdominal facies is present.

Diagnosis. While Delbet believes that the absence of fæcal vomiting is characteristic, many observers mention its presence, and Fantino is careful to note it in two of his cases. The following are the important signs:

1. Great pain, most often centering in the umbilical region.
2. Obstruction and meteorism.
3. Vomiting, usually not fæcal.
4. Slight change in pulse and temperature in the earlier hours.

There is nothing here that will differentiate it from obstruction, and most writers agree that the diagnosis is impossible. Once the abdomen is opened, palpation of the root of the mesentery tells it all.

Prognosis. Absolutely bad without operation. If the obstruction has lasted long enough for the vessels to become thrombosed, the patient will likely die anyway. In my collection of 65 cases there were 23 recoveries.

Treatment. Early median incision, evisceration, and detorsion. If the intestine will not permit of manipulation, first puncture, empty, and suture. In favorable cases a plastic operation to prevent recurrence (Philipowicz) might be thought of.

BIBLIOGRAPHY

CARL ROKITANSKY. Handbook of Pathological Anatomy.
LEVEQUE. Intestinal Occlusion by Rotation of the Intestine. Thèse, de doct., Par., 1885.
HERTING, JOHANNES. Dissertation, Kiel, 1888.
ZOEGE VON MANTEUFFEL. Samml. klin. vortr., 1889, No. 260, 1421.
SCHREIBER. Ztschr. f. klin. Med., 1889, xxxviii, 426.
RICHTER, CARL. Monograph, 1901.
BURGESS, ARTHUR. Lancet, Lond., ii, 1690.
PHILIPOWICZ, W. Arch. f. klin. Chir., pp. 679–735 and 897–945.
VAUGHAN, G. T. Am. J. M. Sc., 1903, xv, 799.
WHITING, A. D. J. M. Sc., 1904, p. 1072.
BATUT. Bull. Soc. méd. chir. de la Drome Valence et Par., 1904, xv–xviii.
PHILIPOWICZ, W. Arch. f. klin. Chir., 1905, lxxvi, 934–960.
KÜTTNER. München. med. Wchnschr., 1905, iii, 482.
CLEMENT, PIERRE. Bull. Soc. Anat. de Par, 1905, lxxx, 737–740.
LERDA, G. Il Progresso Medico, Torino, iv, 90.
LAWSON, C. B. J. Royal Army M. Corps, Lond., 1906, vii, 593.
DANIELSON, WILHELM. Beitr. z. klin. Chir., 1906, xlviii, 100.
ALGLAVE, P. Presse mèd., 1906, xiv, 581.
VAUGHAN, G. T. Am. J. Obst., 1907, p. 56.
BULL, P. Bull. et mém. soc. de Chir. de Par., 1907, N. S. xxxiii, iiii.
LENNANDER, K. G. Deutsche Ztschr. f. Chir., xxxvi, 1.
TESSON, RENÉ. Bull. et mém. soc. de Chir. de Par., 1907, p. 578.
HUTCHINSON, JONATHON. Clin. J., Lond., 1907, xxx, 113.
SCHULTZE. Deutsche med. Wchnschr., 1907.
LERDA, G. Riforma Med., xxiv, 177.
BLECHER. Deutsche Zentralbl. f. Chir., Leipsic, xcviii, 521.
COSTA. Clin. Chir., 1909.
BRUNSWIC LE BIHAN. Presse mèd., 1909.
BILLINGTON, WM. Lancet, Lond., 1909, i, 678.
WILLE, H. Norsk Mag. f. Lægevidensk, 1910, viii, p. 30.
FANTINO, G. Il Morgagni, Milano, 1911, xlviii, 743.
NEWTON, H. A. S. Australian M. J., i, No. 120, 11.
BOSQUETTE. Dauphine med. Grenoble, 1912, xxxvi, 217.
PHILIPOWICZ, W. Arch. f. klin. Chir., 1912, xcvii, 884.
MICHAELIS, P. Wien. klin. Rundschau, 1913, Sept. 21.

CAUSAL FACTORS IN THE DISPOSITION TO CANCER IN OLD AGE[1]

By HOFRAT DOCTOR A. THEILHABER, Munich, Germany

A LARGE series of portions of skin and mucous membranes in individuals of different age were compared in order to ascertain why old people are so frequently attacked by cancer. Many variations were observed, some of which were already known from the study of anatomy but which have not so far been mentioned in connection with the origin of cancer. Thus, connective tissue shows characteristic differences at various ages. In the fœtus it has a remarkably large number of cells, the intercellular substance being very scanty. In the infant the percentage of cells in the connective tissue gradually decreases, while the intercellular substance increases. With advance of age, the number of connective-tissue cells decreases (Figs. 1 and 2).

Atrophy of the cells and a diminution in their proliferative power occur together with a decrease in their number, and, *vice versa*, an enlargement of the cells and cell nuclei and an increased proliferative power take place with an increase in number. Epithelium, on the other hand, does not usually show any marked retrogressive metamorphosis.

Basing our opinion on these observations, we may state that the intensity of a disposition to cancer is in inverse ratio to the number of cells found in the connective tissue.

A second difference is found in the behavior of the blood-vessels. The supply of the healthy tissue with blood is the more abundant the younger the individuals. Exceptions at times are caused by the more or less intense activity of the blood-forming organs. The walls of the blood-vessels, as a rule, are thin in young individuals, the lumina relatively wide. The opposite holds good in old people, the vessel-walls becoming thickened, the lumina smaller. Here also the conclusion may be drawn that the disposition to cancer is in inverse ratio to the blood supply of the tissues.

If organs which have been invaded by cancer are examined, we usually find in the connective tissue about the growth very few cells, blood-vessels stenosed and with thickened walls, and signs of endarteritis obliterans (Figs. 3, 4, and 5). An exception to this is noted, however, in that the tissues immediately surrounding the outermost proliferations of the cancer show a more or less marked reactive hyperæmia with cell infiltration, usually of slight extent.

I drew the conclusion from these and many other similar observations that the local disposition of aging tissue to carcinoma, results from a diminution of the cellular elements and a contraction of the blood-vessels in the connective tissue.

However, these changes alone do not suffice to excite an unlimited proliferation of epithelium. Other disturbances are usually present in those regions of the body subject to malignant invasion. Thus, scars and chronic inflammations, above all, belong to the precancerous state. Very few cells, and a limited number of usually constricted blood-vessels, are also found in old cicatrices and in tissues which have suffered for a long time from chronic inflammations (Fig. 7).

I explain the process of development of cancerous degeneration as follows: Epithelium does not transgress its borders under normal conditions, because the connective-tissue cells protect themselves by defensive bodies against any such invasion. Epithelial proliferation, however, is facilitated if the fixed cells, lymphocytes, and other elements making up connective tissue are scarce and atrophic, especially if this cellular atrophy has become highly marked at a given place on account of cicatricial changes or long-continued inflammatory processes. Then if senile atrophy also becomes associated with such conditions the epithelial cells have an easier battle for existence. They penetrate into the connective tissue, whereupon a round-celled infiltration appears, together with an increase of the protective measures against epithelium. Thereby an additional

[1]Translated by Henry Schmitz, M. D., Chicago.

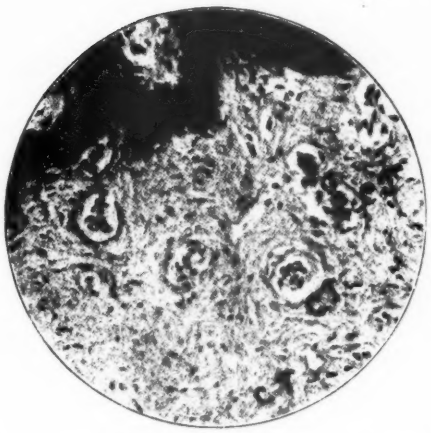


Fig. 1. Dark portions, epithelium; C. T., connective tissue.

Fig. 2. Connective tissue showing decrease in cells.

barrier against the further advance of the epithelium is created until the "battle for existence" generally terminates with a victory for the connective-tissue cells. The erection of new defensive walls and the advance of additional forces for the protection of the connective-tissue territory becomes more difficult for the organism in proportion to the local anæmia and the imperfect blood-vessel dilatation due to atheroma, to say nothing of impaired circulation, deficient cellular metabolism, and decreasing activity of the heart. All these factors appear in organic old age, in scars and in chronically inflamed tissues, but are particularly significant when several of them are combined. It follows, then, that if the connective-tissue cells succumb in this battle, the barrier against unlimited epithelial proliferation is removed. Still other factors contribute to the development or origin of cancer. A deterioration of the tissue fluids, a "humoral disposition to cancer," is present in the majority of cases.

All my investigations convince me that the connective-tissue cells, leucocytes, and lymphocytes antagonize epithelial cells. It is necessary, therefore, to study the variation in structure and the functions of the blood-forming organs in their relation to the disposition to cancer. I began my investigations in the central *abbatoir* of Munich, where the best opportunity was offered to study the internal organs of healthy animals of different ages. I soon convinced myself of the fact that the disposition to cancer is in inverse ratio to the development of the blood-forming organs in the different age periods. The variability in the development of Peyers' patches in the intestine is of especial interest. While they are very prominent and immediately noticeable in young animals, they are so highly atrophic in the old that they must be looked for. The spleen, not changed by disease, undergoes a marked atrophy with advancing age, the trabeculæ project on the cut surface, the follicles grow smaller and poorer in nuclei. The lymph-glands also become smaller with advancing age; the lymphocytes become sparse within the meshes of the reticulum; the parenchyma is in many places replaced by adipose tissue. Atrophic conditions are also found in the bone-marrow with advancing age. The marrow is red and lymphoidal in youth, later changing to a fatty marrow, poor in cells, and it appears as a colloidal marrow in old age; i. e., a gelatinous change of the fatty marrow with a somewhat darker yellow color. The activity of bone-marrow is somewhat lessened in advanced age, and an atrophic condition of the whole blood often occurs. These facts, for the most part already known to the anatomist, have not been emphasized in connection with the origin of cancer. Therefore, I con-

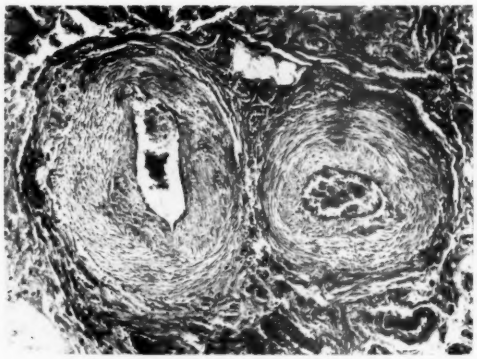


Fig. 3. Blood-vessels in the neighborhood of a carcinoma in a nulliparous uterus.

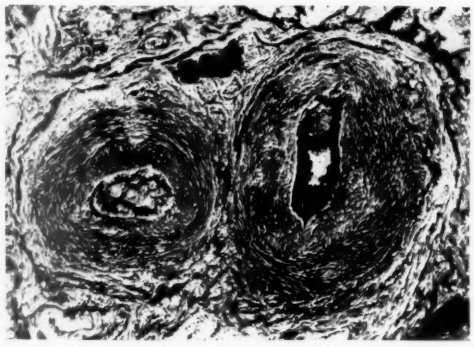


Fig. 4. Nulliparous uterus; blood-vessels about the carcinomatous tissue.

clude that the younger the individual and the better the development and function of the blood-forming organs, so much less is the inclination to cancer.

A cancer can, as a rule, originate only in people in whom local and humoral disposition is present. The local age disposition consists, according to the above statements, in a decrease in the number of connective-tissue cells and in their blood supply, the results of an atheromatosis of the blood-vessels. The humoral disposition to cancer is largely due to an atrophy of the blood-forming organs which occurs in different individuals in varying degrees of severity.

THE PREVENTION OF POST-OPERATIVE RECURRENCE

After removal of a cancerous tumor with the knife or by radiotherapy, a new growth forms in the majority of cases in a relatively short time. In more than three-fourths of the cases it arises in the region where the primary cancer was located. Many physicians assume that by far the most of these recurrences arise from small cancer parasites which were left behind. It is certain that this is a frequent cause of recurrence, but I believe that cases are not very rare in which carcinoma recurs as a result of still other causes. In my opinion, they arise not only from a continued existence of a local predisposition, but the operation may even increase this local tendency to the growth of cancer, since the operation scar consists of tissue quite similar to the atrophic structures from which the cancer tends to originate. As it is a settled fact that every extensive scar predisposes to cancer, we cannot see why a scar caused by operation should be an exception to the rule. It becomes poor in connective-tissue cells and blood-vessels when it grows older, and the continued existence of the "humoral disposition" has a marked influence upon the development of recurrences.

The observation that there may be recurrences in places distant to the operating field, aside from any preëxisting metastasis, is best explained by the humoral disposition. As such recurrence is favored by traumatism and similar influences, the origin can be explained in the simplest manner by accepting a "cancer disease" in which the tumors arise at the place of least resistance. Thus, for instance, Volkmann observed after a breast amputation a recurrence on the parietal bone as the result of a fall on the head. E. Vix reports a recurrence on the vertex after an operation for cancer of the abdominal wall, in a laborer who carried loads on his head. After an amputation of the thigh for sarcoma Cohnstein saw a recurrence, not in the scar, but in the gluteal regions which were exposed to a continuous pressure.

Proceeding on the theory that the majority of recurrences are caused by leaving behind cancer-germs, surgeons have attempted to remove all cancer-cells by excising the cellular

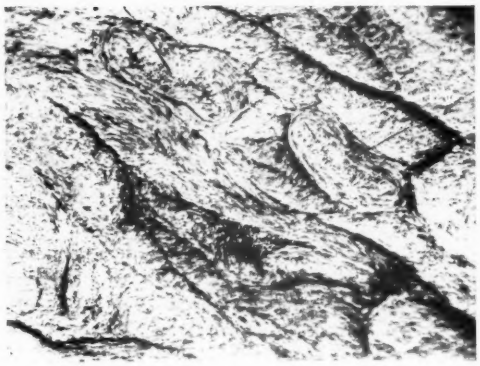


Fig. 5. Nulliparous uterus with carcinoma vessels about the carcinoma. B. V., blood-vessels.

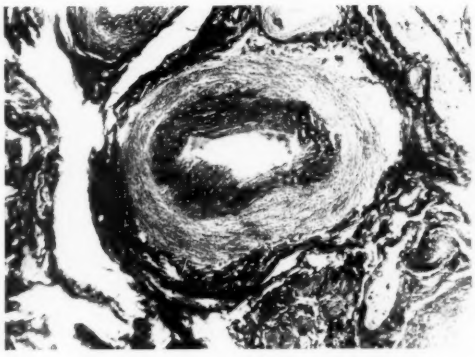


Fig. 6. Carcinoma of uterine body; blood-vessels in the surrounding tissue.

tissue and the lymphatic glands as far away from the growth as possible. They have endeavored to operate in the most radical manner. The result of this has been an increased mortality ratio after cancer operations, and the reduction in frequency of recurrence is on the other hand but slight.

I claim that a considerable reduction in recurrence can never be attained by a more and more extensive extirpation of the surrounding tissues of the cancer. The removal of the local and humoral disposition of the patient, i. e., the cure of the cancer disease proper, seems to be more successful. If one would extirpate the toe on account of a frequently recurring gouty swelling, a cure would only exceptionally result from a change of metabolism caused by the operation or from any other cause. The gouty swelling would sooner or later appear at another place in the body, perhaps in the region of the scar. If we expect to cure gout, we must attempt to change the entire body fluids by diet, abundant bodily exercise, baths, etc.

The conditions are similar in many cases of cancer. Here also the condition of the blood must be improved just as well as the local power of resistance toward epithelial proliferations must be increased. To attain the latter, I attempt to produce an increased proliferation of connective-tissue cells, and a marked infiltration of this structure with leucocytes and lymphocytes by nutritional improvement of the blood. This can be obtained by definite methods of hyperæmizations which may be performed by various means such as Bier's hyperæmic treatment, massage, etc. The diathermic method as introduced by Nagelschmidt and Zeynek has proved the most efficient. It also produces a marked hyperæmia in places which are far removed from the point of application of the electrodes.

If an organ is treated for a long time with diathermy the vessels dilate and the tissues hypertrophy, according to my observations. This dilatation of the vessels and hypertrophy of the tissues lasts many months. Besides these, an increased accumulation of round cells in the connective tissue is found after frequent use of diathermy, and the connective-tissue cells proliferate markedly. Conditions arise, therefore, exactly the reverse from those in the beginning of cancer. We see correspondingly good results in the after-treatment following cancer operations. The scars remain red, become rich in blood-vessels, round cells, and connective-tissue cells. I use diathermy periodically during each year two or three times, in eight to ten séances of fifteen minutes each. At the same time, I give subcutaneous injections of certain organic preparations (spleen, uterus, thymus) near the scar. A marked venous hyperæmia is thereby caused in the immediate surroundings of the scar which lasts for a number of days. Besides the marked dilatation of the blood-vessels, a considerable round-celled in-

Fig. 7. E., epithelium. C. T., connective tissue.

filtration was seen on microscopic examination at the injected places in rabbits. These injections have the advantage that they favorably influence the humoral disposition. According to my investigations, the changes in the body fluids which permit cancer formation are largely brought about by defective function on the part of the blood-forming organs. The injection of certain organic preparations, particularly of the thymus, the spleen, and the uterus, increases the activity of the blood-forming organs, resulting in a marked leucocytosis which renders the formation of epithelial proliferation difficult. Diathermy may also be used to increase the function of the hæmatopoietic organs. Therefore, I treat the spleen several times yearly in a number of sittings with the diathermy apparatus. This is followed by a marked increase in the number of leucocytes in the blood. A sojourn in high altitudes, the avoidance of alcoholic beverages, the use of vegetarian diet, salt and mud baths, and active and passive exercise have proved of benefit.

The genital glands (ovaries and testicles) act apparently favorably on the development of cancer, their influence being "cancrigenous" while the blood-forming organs possess "cancrilytic" action. Therefore, I attempt to produce an atrophy of the sexual glands by röntgen treatment in women who are still menstruating. Recurrences after breast amputation is more readily prevented if the ovaries are destroyed, the clinical experience which different operators had had with castration in inoperable carcinoma coinciding with this fact. Whether it would be rational to castrate men under these same conditions would have to be demonstrated by clinical experiments.

I perform venesection in all patients from whom cancer has been extirpated, removing 300 to 400 ccm. of blood twice yearly. This markedly stimulates the activity of the blood-forming organs. I often successfully resort to venesection in people 70 to 80 years old. Fischera reported at the Cancer Congress held in 1913 at Brussels that he could confirm the beneficial action of venesection proposed by me as a prophylaxis against cancer recurrence, basing his allegation on experimental investigations. If he bled mice, the resistance against inoculation with cancer grew, due to the increased activity of the hæmatopoietic organs.

I begin the hypersensitization during the third month following the operation; that is, at a time when the scar begins to atrophy.

The described after-treatment has still another very agreeable side effect; the subjective well-being soon improves during treatment.

The patients often complain of abdominal pains, backaches, discharges, etc., after extirpation of abdominal cancers. These symptoms are caused by the scars and by the disturbances in the circulation of the blood due to the scar formation. All such annoyances improve considerably after the induction of hyperæmia. After operations on the breast, pains in the scars and limitation of motion of the arms often persist. An essential improvement tends to take place after hyperæmic treatment, which might advantageously be combined with massage.

The influence of hyperæmic treatment can also be demonstrated objectively. It may best be seen in those scars which are easily exposed to inspection; for instance, in those after breast amputations. The scars are entirely different from those obtained under ordinary conditions. They are not

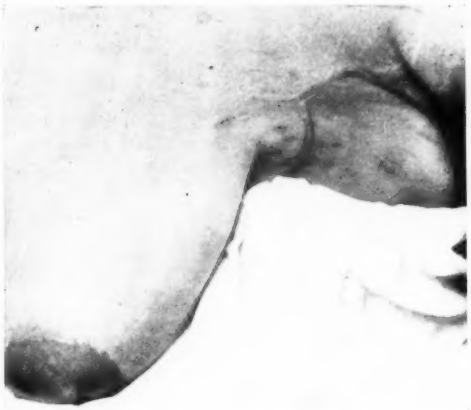


Fig. 8. Shows hyperæmia and hypertrophy of the scar of a patient who was operated on two years ago and treated frequently with diathermy and venesection. The suture canals lying close to the axilla were not covered by the broad electrode during the diathermization. They are very pale and readily distinguishable by their color from the medium red suture canals covered by the electrode. The hypertrophy of the tissues was also absent in the peripheral suture canals. Note that intervals of four and six months exist between the days the photographs were taken and the last treatments by diathermy.

Fig. 9. Shows the opposite; viz., the condition of the scar of a patient not treated afterwards. The scar is so pale that it is recognized with difficulty. It is highly atrophic like all old scars.

pale but red, as during the first months after operation. They frequently show a keloid-like hyperplasia of the tissues, remain movable on their substructures, and do not contract to any extent. It is very improbable that such changes in the histologic structure of tissues threatened most with recurrences should not favorably influence the prevention of a recurrence.

My results are as follows: Of seventy-two cases of cancer coming for treatment during the last five years I operated radically upon thirty-seven. Twenty-four of these submitted to a long-continued hyperæmic treatment. Twenty of these are at present still free of any recurrence; three died during the first year following the operation from metastases of the internal organs; a fourth contracted a local recurrence to which she succumbed. Of the twenty well patients, six were operated upon five years ago, and five, four years ago. Christoph Müller (Immenstadt) has treated during the last four years a series of twenty cases of mammary cancer in a similar manner, without a single recurrence. Seven of these patients were operated upon more than four years ago. They all were at the limit of operability. Altogether, eighteen cases treated four years ago and six treated five years ago are free from recurrence.

The method of my after-treatment of cancer patients following operations ought to be one of the most important advances which has been made for some time in the field of cancer treatment, judging from all I have seen during observations covering five years. An especial advantage of this method is that the family physician can coöperate in the work of preventing recurrence. Bier's hyperæmic treatment and the injection of organic extracts can be given by any physician.

A discussion of the value of this after-treatment following cancer operations by X-rays finally remains. It is intended either to destroy tumor remnants left behind, or to prevent the development of a new cancer or to heal developing recurrences. In the first

case the X-rays will have to be used immediately following the operation; in the second and third instances it will be necessary to use the rays intermittently for years at definitely timed intervals. Remnants of tissue may be destroyed by the diacutaneous method if primary union is desirable. Success will be obtained in only a very small number of cases. The probability of success is greater when the rays are applied through an open wound. In such cases, where we do not suture on account of a plastic operation to be undertaken at a later date or for other reasons, it is advisable to leave the wound open for a longer or shorter time and to expose it intensively to the X-ray. However, Werner, who often used this procedure, reports that it does not positively protect against recurrence. Concerning frequent prophylactic, intermittent X-ray therapy to bring about the immediate destruction of beginning recurrences, I do not believe that any great number of successful results can be obtained thereby. I refer to the communications of Heinecke, whose investigations were corroborated by Krause, Aubertin, and others. He showed that the blood-forming organs are very much endangered by intensive use of X-rays. The cells of the bone-marrow, spleen, and lymphatic tissues react markedly to röntgen and radium rays producing a degeneration of the nuclei. The number of the lymphocytes and leucocytes decreases to subnormal, after a transient polynuclear leucocytosis, to recuperate only slowly. The blood-cells cannot be protected by a filter technique, as they are attacked especially by the harder gamma rays passing through the metal filter which we need for applying X-rays. The blood-forming organs undoubtedly recuperate from the disturbances caused by the rays. However, if the rays must be used again and again, recuperation ultimately ceases.

Considering the great importance a perfect function on the part of the blood-forming organs possesses as a prophylaxis against cancer, it is not probable that by means of the sole use of radiotherapy the percentage of recurrences is markedly decreased. If one wished to destroy with a probable certainty beginning recurrences before they become macroscopically recognizable, then the X-ray must be used several times a month for many years. Experience in "röntgen-cancer" has shown that the disposition to cancer is directly increased by the too frequent use of the rays. If the rays are used very diligently after operations, the cancer disease is frequently aggravated and a recurrence is probably directly excited. If the rays are not used very frequently, then it must be a coincidence if one does hit a recurrence which is not yet macroscopically recognizable and thus prevent its growth.

The communications so far reported about the frequency of recurrences after X-ray treatment seem to verify the correctness of this evidence, especially for the non-gynecologic cancer. Heidenhain reported at the tenth congress of the German Röntgen Society at Worms, in 1914, that the prophylactic use of X-rays has not markedly decreased cases of recurrence. Similar reports were made at the meeting of Natural Scientists and Physicians in Vienna in 1913.

DEPARTMENT OF TECHNIQUE

A NEW AND RAPID METHOD FOR OPERATING UPON IMPASSABLE URETHRAL STRICTURE

By CHARLES H. CHETWOOD, M. D., LL. D., New York City
Professor of Genito-Urinary Surgery, New York Polyclinic; Visiting Surgeon to Bellevue Hospital

THIS technique has already been reported, but continued experience in its use has strengthened its claims in my estimation as a reliable method in certain cases. All operators come in contact with a varying percentage of cases of impassable stricture, by which is meant impassable to any instrument in the hands of the particular operator, whether or not the flow of some urine may be possible. This percentage is to a certain degree a personal equation, and therefore the adoption of this technique is also more or less governed by the same factor. Personally, I have never been compelled to perform suprapubic cystotomy for retrograde approach to the urethra, owing to an unsuccessful attempt to find the urethra by way of the perineum. But I must own to having been in some very critical situations, involving the expenditure of a laborious length of time, in attempting external urethrotomy without a guide for impassable stricture. And in certain cases this difficulty has been as much in finding the distal or anterior section of the urethra as in locating the proximal or posterior end. For the latter, the method suggested by Young, of reaching the apex of the prostate, may be used most effectively. It is not, however, from this point, in my hands, an easy matter to find the curve of the urethra anteriorly, in cases where the stricture area is exceedingly tortuous and buried in nodular tissue. The intermediate portion may be resected, and the finding of the distal or anterior portion materially facilitated by injecting an aniline fluid through the meatus, to stain the urethral tract at the site of the perineal wound. But this attempt is not always effective, when pockets and false passages exist.

The technique in question was originated by the chief of my staff, Dr. D. A. Sinclair; the application we have mutually employed. The result is a complete mastery of the difficulties of an otherwise troublesome complication.

It is desirable that the patient retain urine for several hours previous to operation. This is obviously unnecessary in cases of complete retention. The operation is performed under local or general anæsthesia, as preferred. A cannula and trochar, about 16 French caliber, is thrust just over the pubis in the median line, into the bladder, with the latter under distention, either with urine or antiseptic fluid forced through the urethra. When the trochar is removed, the fluid is emptied and the bladder is cleansed as before a cystoscopy. Now, through the cannula is introduced an indirect lense telescope of proper caliber to fit the tube. Through this the internal orifice of the bladder is viewed with absolute clearness. The distal aperture of the cannula is then applied to the internal orifice, the telescope removed, and a curved, flexible obturator is introduced through the cannula, which readily enters the prostatic urethra, and may be advanced as far as the apex of the prostate, or even the membranous canal. A finger introduced into the rectum determines the success of the procedure.

The flexible obturator is provided with a fine interior lumen, through which a filiform or whalebone bougie may be introduced, which often finds the proximal opening of the stricture, and then may be advanced until it appears at the meatus. In such instances the remaining steps of the operation are much simplified. A perineal cut is made on the point of the obturator, the bougie guide is drawn through the perineal opening, and a small urethrotome knife with an eyelet is fed thereupon, toward the anterior section, and the strictured area is incised. In cases where it is not found possible to advance the bougie to the anterior urethra, the method of injecting an aniline blue solution is adopted, but through the canal of the obturator, while it is applied directly to the point of obstruction. In either of these instances the performance of the operation is simplified, and, as compared with the older methods of suprapubic retrograde urethrotomy or perineal section without a guide, its duration is suprisingly short.

THE STUDY OF CHRONIC INTESTINAL STASIS BY MEANS OF THE RÖNTGEN RAYS[1]

By GEORGE E. PFAHLER, M. D., Philadelphia

So much excellent work has already been done upon the subject of intestinal stasis by such men as Lane, Jordan, Bainbridge, Quimby, Leslie, and many others, that it would seem hardly necessary to write more. The importance of the subject, however, and the lack of thorough appreciation by the general profession, will probably justify my effort.

The symptoms which result from chronic intestinal stasis have been previously summarized by Bainbridge as follows: "(1) Headache, severe and frequent; (2) nausea, followed by retching or vomiting; (3) anorexia, almost constantly present; (4) loss of weight; (5) coldness of extremities; (6) mental apathy; (7) constipation; (8) foul taste in mouth, often accompanied by foul breath, carious teeth, and furred tongue; (9) abdominal distention, relieved by eructation, the passage of flatus, or an action of the bowels; (10) abdominal tenderness over the areas of fixation; (11) skin-staining; (12) breast changes, simulating chronic mastitis, in the early stages, and cystic degeneration in the later stages; (13) general muscular pain and more or less marked stiffness of joints."

The diagnosis of chronic intestinal stasis can be suspected from the clinical symptoms, but the definite cause and location of the stasis can be determined only by means of the röntgen rays, or by a rather extensive exploratory operation.

In the consideration of this subject, stasis caused by obstruction due to malignant disease will not be considered.

TECHNIQUE

In the study of intestinal stasis, I believe that it is best not to disturb the usual routine in the life of the patient more than is absolutely necessary. Therefore, at the beginning of this study the patient should not be purged, should not be starved, and should not be interfered with in the quantity, quality, or time of the usual meals, for by so doing one creates more or less artificial conditions, which may lead us to overlook stasis, or to observe mechanical conditions which may have no real influence upon the symptoms of the patient.

Laxatives. If the patient has been accustomed to laxatives daily, it is probably well to allow this to continue up to within twenty-four hours of the beginning of the examination. In extreme cases it may be well even to continue it during the study, for by so doing one may often recognize how ineffectual the customary laxative is, and why.

In the early case, or where the patient has moderate symptoms, it is usually well to omit all laxatives during the examination, and for twenty-four hours previous. Patient should be allowed to eat his usual breakfast. One hour later, he should be given, as recommended by Jordan, a glass of water containing four ounces of bismuth subcarbonate, and a half-ounce or more of sugar of milk. (Jordan recommends one and one-half ounces, but this amount seems to have caused diarrhœa in several patients that I have examined.)

By manipulation of the stomach the bismuth can be made to mix thoroughly with the partly digested food. The stomach can then be clearly outlined, and a fair idea obtained of its position, size, and motility. Even gross defects can be detected by this process. Spasmodic contractions, when present, may also be recognized. I believe this is not the best mixture for the study of gastric ulcer and carcinoma, or for duodenal ulcer.[2]

The patient is examined first fluoroscopically in the vertical posture, and as many röntgenograms are made as seems necessary in each particular case. The patient is then placed upon the fluoroscopic table, and examined fluoroscopically in the supine position. He is then turned in the right lateral, which permits complete filling of the duodenum. The patient is then quickly turned on his back, and the duodenum is either examined fluoroscopically or a röntgenogram is made; and this process may be repeated until satisfactory evidence is obtained of the conditions present. One may find dilatation and stasis either in the first, second, or third portion of the duodenum. By this means one recognizes the extent of the obstruction caused by mesenteric attachment at the duodenojejunal junction, as described by Jordan.

If the stomach seems to be emptying itself with abnormal rapidity, a second examination should be made at the end of three hours. If it

[2] The dangers of fluoroscopic examinations must not be forgotten. See "Present-day Dangers of Röntgen Ray Burns, and How to Prevent Them," J. Am. M. Ass., 1914, Jan. 17.

[1] Read by invitation before the Eastern Medical Society of the City of New York, illustrated with lantern slides, May 8, 1914.

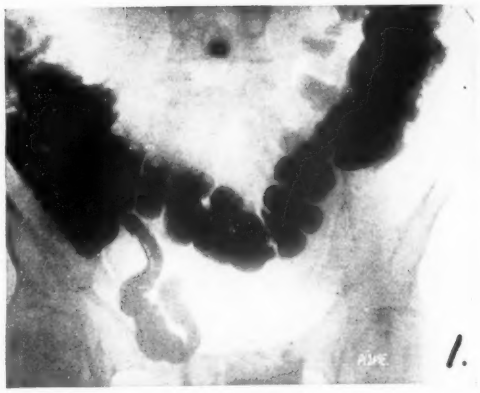


Fig. 1. Shows retention in the ileum, twenty-four hours after a bismuth meal, due to a kink.

Fig. 2. Shows stasis in the cæcum and ascending colon with cæcum mobile.

is emptying at normal rate, or is delayed, a second examination should be made at the end of six or more hours. At the six-hour examination, normally, the food should be in the terminal coils of the ileum, and in the cæcum and ascending colon. A third examination may seem advisable at the end of from nine to twelve hours, at which time, normally, the head of the bismuth column should have reached the splenic flexure, or probably, in small fragments, even the rectum. Another examination should be made at the end of twenty-four hours, at which time, normally, the bismuth mixture should have been passed, or should be found in the rectum, sigmoid, and transverse colon.

Stasis may at times be recognized in the coils of the small intestine, such as occurs at times in extensive adhesions following an old peritonitis. Generally, however, the first evidence of stasis is recognized in the terminal coils of the ileum. I believe one cannot look upon retention in the terminal ileum as evidence of stasis unless it is present at the end of nine to twelve hours. Stasis in the terminal portion of the ileum may be due to kinks, such as have been described by Lane, or to adhesions, which are generally secondary to a chronic appendicitis; or it may be due to either organic or spasmodic constriction of the ileocæcal valve. I have seen cases of spasmodic constriction of the ileocæcal valve cause retention in the terminal coils of the ileum for more than twenty-four hours. The presence of the Lane kink in this region can be determined by examining the patient in both the vertical and recumbent postures, which procedure, by the difference in the positions, will cause a variation in the outline of the coils of the terminal portion. If it is due to adhesions, one will find difficulty in separating the various coils of the ileum, or in moving them about at will. One may at the same time be able to recognize other evidence of adhesions, such as fixation of the appendix, immobility of the cæcum, or fixation of the cæcum in certain directions. Cæcum mobile is recognized by this same procedure. Retention in the ileum may also be due to a patulous ileocæcal valve, which permits reverse peristalsis to cause backward pressure in the ileum.

Stasis in the cæcum and ascending colon is recognized by the retention of the bismuth mixture in this portion of the bowel in from twenty-four hours to many days. It may be due to a kink which has formed at the hepatic flexure, or it may be due to a mass of adhesions secondary to gall-bladder disease, or secondary to a perforating gastric or duodenal ulcer, as I have observed; or it may be due to a Jackson membrane, which in some way seems to interfere with the peristaltic action. If it is due simply to a kink, one may differentiate it by injection of the colon in the supine posture, in which event the colon will fill freely, or can be made to fill freely by slight manipulation. The lumen of the colon can be shown to be complete; whereupon, if the patient assumes the vertical posture, the kink reforms and can be demonstrated. If the disturbance is due to a mass of adhesions, one may be able to find that the transverse colon cannot be separated from the

Fig. 3. Shows stasis in the cæcum and ascending colon, and in the first portion of the transverse colon.

Fig. 4. Same case as No. 3. Shows obstruction at the same region, with colonic injection, both due to a Jackson membrane.

Fig. 5. Shows stasis in the transverse colon, forty-eight hours, due to obstruction at the splenic flexure.

ascending colon; or there may be a reduplication in the first portion of the transverse colon which cannot be straightened out; or the entire hepatic flexure may be fixed securely. Then, too, one may be able to demonstrate the presence of the primary cause of such adhesions, such as gastric, duodenal, or gall-bladder disease.

Stasis in the ascending and transverse colon may be due to stenosis at the splenic flexure. This stenosis may be caused by a kink, or may be due to a mass of adhesions, which sometimes causes a constriction in both the terminal portion of the transverse colon and the first part of the descending colon. In such instances a gas valve is produced at the splenic flexure. Such patients complain of a great deal of distress in the left hypochondriac region, vague pains and flatulence; the patient tries to eruct gas from the stomach, which of course gives no relief, since the gas is not in the stomach, but seems to give the sensation of gas in the stomach. In these cases the diagnosis is rarely made, and often is not even suspected until a röntgen examination has been made.

Fig. 6. Same case as No. 5. Shows obstruction at the splenic flexure through a colonic injection. You will notice the great accumulation of gas under the left side of the diaphragm. The colonic contents had to pass through the first constriction into this gas chamber, become liquefied, and then work their way gradually into the descending colon.

Fig. 7. Shows obstruction in the descending colon due to a kink. This patient developed recurring attacks of colonic obstruction covering a period of one week in four. No organic lesion was found at operation. Notice the abrupt termination of the colonic injection: the bismuth above this point is in the small bowel.

Obstruction at the splenic flexure and *stasis in the transverse colon* may also be caused by splenic loops. These loops consist of elongation of the colon in the region of the splenic flexure, which permits an accumulation of gas, and twisting of the colon; this temporarily blocks the progress of the colonic contents. In my experience the descending colon rarely remains filled for any length of time, because reverse peristalsis in this section of the bowel is very active; and when there is any obstruction to the onward flow of the colonic contents, I believe they are carried back into the transverse and ascending colon. Therefore, stasis in the transverse and ascending colon may be due to some obstruction at the sigmoid flexure or rectum.

The effect of this reverse peristalsis is experienced by almost everyone from time to time, because all have experienced the intense desire for stool at an inconvenient time, and then this necessity entirely disappears. The disappearance of this desire is due to the reverse peristalsis, which carries the contents back into the ascending and transverse colon.

Obstruction to the flow of the colonic contents through the descending colon may be due to spasms, adhesions, neoplasms, kinks, or twists. The presence of adhesions is recognized, after injecting the colon, by fixation of a portion of the bowel. Spasms are recognized by the clear-cut lines separating the bismuth content of the bowel very much as the pyloric sphincter separates the contents of the stomach from those of the duodenum, normally. In fact, I have observed these spasmodic constrictions in the descending colon more often than in any other portion. I believe that these spasmodic constrictions are reflex, but I do not yet know their causes.

Neoplasms tend to separate the lumen over a definite portion of the bowel, either by pressure from without or by growth within the lumen.

Kinks can be recognized because they develop only in certain positions; and when the position is

Fig. 8. Shows a sigmoid loop which rises to the level of the diaphragm and causes periodic attacks of intestinal obstruction, which were usually interpreted as sick headaches.

Fig. 9. Shows retention after the bowels were supposed to be thoroughly empty, and also shows a sacculation and retention in the descending colon and the cæcum down in the region of the rectum. This patient complained for twenty years of a constant desire to go to stool, probably due to the pressure of the cæcum upon the rectum.

varied sufficiently during the examination, these kinks can be released.

Obstruction at the sigmoid is more likely to be due to kinks, adhesions, neoplasms, or twists, occurring in connection with a redundant sigmoid.

Kinks may cause definite localized obstruction to the oncoming bismuth column, but one cannot conclude that such kinks, or obstructions, are absent simply by following a bismuth meal from the mouth, because of the reverse peristalsis, which may cause this portion of the bowel to be completely empty at the time of examination. I believe that these kinks more often result from a redundant sigmoid, which produces the sigmoid loops, the tops of which may at times reach the diaphragm; and when this loop becomes distended with gas, it may not only cause a kink at the sigmoid flexure, but may cause pressure upon the transverse colon and upon the stomach, causing temporary obstruction at these two or three places. In other instances the sigmoid loop may extend across to the right side of the abdomen. Such a loop may be present for a long time without giving rise to symptoms, but if the abdomen relaxes from some acute illness, from pregnancy, or from emaciation, the bowel is permitted to dilate, and then evidence of obstruction and stasis, with exaggeration of all other symptoms, follows. I believe that these loops are not a normal condition, but that they may be present in healthy people. I have never found them, however, in anyone not suffering from some abdominal or toxic symptoms.

The sigmoid is also a favorite location for neoplasms. Adhesive bands following inflammatory conditions within the pelvis are also frequent. When adhesive bands are the cause of the symptoms, one has difficulty in separating, and moving freely, the sigmoid and upper portion of the rectum.

Stasis within the rectum may be due to spasms of the anal sphincter, to actual organic obstruction, or, more commonly, to a torpor or loss of sensation of desire for stool. I commonly find the rectum greatly distended with fæcal matter, and yet the patient has no desire for stool and not the slightest sensation of the presence of this fæcal matter in the rectum. I believe that this loss of the sense of rectal pressure is much more

common than we know, and that it results from carelessness, or modesty, early in life, at which time nature's call is ignored, and is ignored so long and so often that finally the nerves do not respond to this stimulus; and I believe that commonly this is the primary condition causing intestinal stasis. The colonic contents are then dammed back, causing a stretching or elongation of the sigmoid, producing finally these large sigmoid loops, with the secondary kinks and definite obstruction; in other instances causing elongation of the descending colon and producing loops in the splenic region,— for I am quite sure that the first effect of obstruction of the bowel is elongation of the bowel above the obstruction, and that actual dilatation only occurs late, after atony develops. I can conceive that this stasis and its effects, even occurring farther upward in the bowel, may originate in the rectum. This stasis in the rectum likewise may have its origin later in life, and be secondary to depression, shock, intercurrent illness, or any conditions which would make the patient ignore the call of nature, or that would blunt the nerves so that greater stimulation would be required to bring about the proper reflex.

Finally, in the study of intestinal stasis I believe that in all cases the bismuth meal should be followed through the gastro-intestinal tract; but I believe that in all instances there should also be given an enema, and a careful fluoroscopic and röntgenographic examination made, in both the supine and vertical postures. This will frequently show the cause of the intestinal stasis, which otherwise the surgeon would have to hunt for, or the physician would have to infer.

For instance, the colonic injection will show best the various organic constrictions of the bowel, the effects of the adhesions, the presence of loops; it will also be the means of demonstrating the presence of a patulous ileocæcal valve, which is so often indicative of adhesions and commonly associated with chronic appendicitis.

Fig. 10. Shows colonic stasis, with diverticulitis, in a woman who claimed to have a bowel movement every day, and who was suffering from advanced chronic rheumatoid arthritis.

These röntgenographic examinations, when properly and carefully done, require much time and are of considerable expense, but they give more definite knowledge of the conditions present, and point the way for treatment more clearly, I believe, than can be done even by an exploratory operation.

BONE TRANSPLANTATION AS A TREATMENT OF FRACTURE AND FRACTURE-DISLOCATION OF THE SPINE[1]

With Report and Presentation of Case

By E. PAYNE PALMER, M. D., F. A. C. S., Phoenix, Arizona

TRANSPLANTATION has won such an important place in the treatment of fractures and diseases of bone that the surgeon must consider the procedure in all obstinate and unsatisfactory cases of this kind that come under his care.

In fracture-dislocations of the spine, most of the unfortunates who recover sufficiently to be up are compelled to wear a plaster or leather jacket or some kind of uncomfortable body brace for months or years or even throughout life, in order to secure extension and immobilization of the injured spine. Since the bone transplant has served this purpose so well in other parts of the body and in the spine in Pott's disease, as so admirably demonstrated by F. H. Albee, it seems that it should act just as satisfactorily in the treatment of fractures and fracture-dislocations of the spine. Hence it was that I resorted to its use in a case of this kind, which I will report and present.

The subject of fractures and dislocations of the spine is such an important one that, in this short paper, I will treat it only in a general way, simply to bring out a few of the most important points. Understanding the anatomy of the spine, one can readily see that fracture without dislocation, or the reverse condition, is exceedingly rare. Hence the term "fracture-dislocation" is generally applied to these injuries.

Fracture of the bony structure of the spine is always a grave injury and its diagnosis, prognosis, and management present serious problems to the surgeon. Fracture dislocation usually produces a partial or complete separation of the segments of the cord, so that complete recovery is rare. Regeneration of the non-neurilemmatous elements of the cord does not occur, so, following a division of the cord between the atlas and the first lumbar vertebra, no improvement is to be expected except through extra spinal nerve anastomosis. There is always uncertainty regarding the pathological conditions. The X-ray is of assistance in determining the injury to the bony structure, but unfortunately the extent of the injury to the bony canal is no guide to the damage done the cord. There is but one safe course in all cases of spinal injury presenting deformity and paralysis: that is, to perform an immediate exploratory laminectomy to determine whether operative treatment will improve conditions. We must remember that in all dural and bone work, our technique must be perfect. I wish to emphasize the importance of immediate operation, as delay is dangerous. The cord may be pressed upon by bony fragments or by a blood-clot within or without the dura, which pressure, if relieved at once, will leave the cord uninjured, but if allowed to remain a few days or weeks will result in degeneration. It has been shown at many late operations that the only lesion to the cord was compression, but the late operation was of no avail as the degeneration had occurred. An early operation in such cases would, of course, have relieved the pressure and prevented these degenerative changes.

Case Report. *History.* Mrs. C., age 30. On November 26, 1913, while standing on the sidewalk, was struck forcibly from behind by a motor truck, bending the body forward into extreme flexion, then knocking or rolling her about ten feet. She was not rendered unconscious and remembers a crushing sensation in her back, and, immediately, a very severe pain there which continued until she was anæsthetized at the time of operation. She tried to get up after the accident, but was unable to rise and fell back on the ground helpless. The patient was taken to her room in an auto and seen by Drs. John Wix Thomas, Roy E. Thomas, and Willard Smith, who diagnosed her condition, and, realizing the importance of immediate operative interference in such cases, sent her to St. Joseph's Hospital, where I saw her.

Examination. The patient complained bitterly of pain over the lower dorsal and upper lumbar vertebræ and the slightest movement of the body caused excruciating pain. The lower dorsal and upper lumbar regions, over and around the spinous processes, were ecchymotic, swollen, and very tender. The spinous process of the twelfth dorsal vertebra was depressed inward and freely movable, showing unmistakable signs of being fractured. There was partial loss of motion and sensation in the lower extremities.

Primary operation. An incision was made directly over the injured spinous process. Free hæmorrhage had taken place into the tissues. The supra- and infraspinous ligaments between the eleventh and twelfth dorsal and first and second lumbar vertebræ were lacerated. Both laminæ of the twelfth dorsal were completely fractured and displaced inward, pressing upon the cord, so all that was necessary to expose the cord was to dissect the soft tissues from the spinous process and lift the bony fragment from its bed. The right lamina of the first lumbar vertebra was fractured. Removal of the bony fragment of the twelfth dorsal revealed a cord compressed by angulation

[1] Read before the 23d Annual Meeting of the Arizona State Medical Association at Tucson, Arizona, April 21 and 22, 1914.

Fig. 1. Anteroposterior view of transplant four months after operation, showing transplant over tenth, eleventh, and twelfth dorsal and first and second lumbar vertebræ.

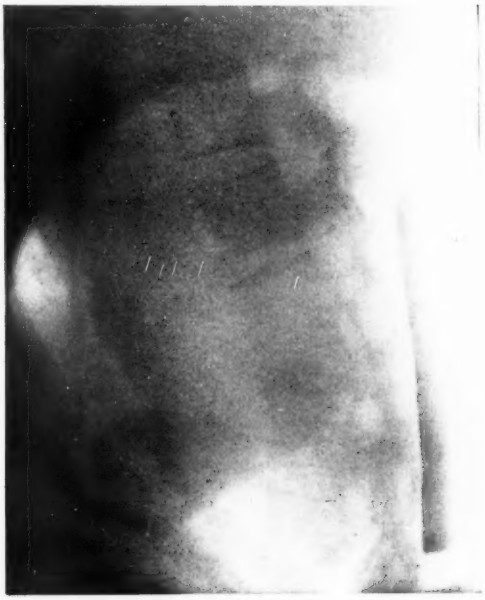


Fig. 2. Lateral view of transplant and spine, showing fracture of last lumbar vertebra with deformity. Radiograph four months after transplant.

of the spinal canal at the junction of the twelfth dorsal and first lumbar vertebræ. (Radiograph shows that this condition was due to crushing of the body of the twelveth dorsal.) The cord compression was relieved by a laminectomy on the first lumbar. The cord soon regained its normal fullness and appeared uninjured. It was punctured with a needle and clear cerebrospinal fluid obtained. The wound was closed and dressed. The patient was kept at absolute rest on her back, supported by sandbags on either side. Recovery was uneventful. Motor and sensory functions returned to normal and there were no bladder or bowel disturbances.

In considering the anatomical conditions and loss of function of this case and thinking of the usual line of treatment by prolonged confinement to bed with plaster cast, jacket, or braces to secure immobilization and extension, and the discomfort incident to this method, I decided that an internal splint by means of a strong bone transplant after the method of Albee for Pott's disease would give an immediate immobilization, support, and extension to the injured spine which could be secured in no other way. If we secured bony union between the transplant and the spinous processes above and below the injury, we would give to the spine a firm supporting power almost up to the normal. If bony union failed to take place, the transplant would unite with the ligamentous structures of the spine, and, at least, furnish temporary immobilization, support, and extension.

Secondary or transplant operation. After we were satisfied that the patient had fully recovered from the effects of the injury, she was prepared for the secondary operation, three weeks after the laminectomy. During this entire time, she had remained upon her back and was in good condition. Albee's technique was followed in a general way in the transplant operation. The original incision was cut through and enlarged above and below. The flaps were dissected back and two spinous processes above the injured vertebræ and two below were exposed. The supraspinous and infraspinous ligaments over and between the two processes above and then those of the two processes below were cut through and separated from the tips of the spines. The supraspinous ligament over the injured vertebra was cut through and the muscle separated to make a bed for the transplant. The four prepared spinous processes were split with a chisel, fracturing about one-third of the spinous process on the left side to a depth of about one inch, and, at the same time, taking extreme care that the right two-thirds of the spinous process was not fractured.

After preparing the bed for the transplant, the wound was packed with gauze soaked in saline solution and the flaps clamped together to protect the wound. With a chisel a strong transplant six and one-half inches by one inch by three-fourths inch, with periosteum and marrow-substance was removed from the crest of the right tibia. The ends of the graft were cut on the slant to prevent sharp edges of bone projecting beneath the skin. A motor saw would have made this work much easier and produced a

a b c

a. Photo showing degree of flexion with lateral rotation four months after transplant.
b. Four months after transplant, showing patient in erect posture.
c. Degree of flexion above and below transplant, four months after operation.

transplant more uniform in size and outline. The transplant was caught and held with two heavy forceps and placed between the split portions of the spinous processes with the periosteum posterior and the two raw bony surfaces in contact with the two raw surfaces of the spinous processes; so the transplant had two chances to unite with each spinous process. The supraspinous ligaments were brought together with interrupted kangaroo tendon sutures which held the transplant firm. The dense tissues were brought together with another row of interrupted kangaroo tendon and the wound closed with deep silkworm-gut and horse-hair sutures. The wound in the leg was closed with a deep layer of gut and horse-hair in the skin. At no time during the operation was the wound touched with the gloved hand or anything which had come in contact with the gloved hand. The technique was perfect, which is necessary in such cases if we are to secure perfect results. The wounds were dressed and the patient again placed on her back in a fracture bed with sandbags on both sides. For several days she suffered acutely from pains in the lower extremities, with exaggerated patella tendon reflex; this was attributed to a mild form of myelitis resulting from trauma to the cord around the previously injured area while splitting the spinous processes with the chisel. Other than this, her recovery was uneventful. She was kept on her back seven weeks, after which she was turned on her sides and allowed to move herself in bed. At the end of another ten days, she was put in a wheelchair and encouraged to increase various body and lower limb movements. She left the hospital twelve weeks after the injury, able to stand alone and walk with assistance. At no time has she had a brace or support, except the regulation style corset which offers no support to the spine. Since the fifteenth week she has walked freely without assistance and has improved steadily, so that, as you see, observers would not detect anything abnormal about her walk, except for the short steps which she takes and a slight halt in the right limb.

Necessarily, she has some limitation of flexion and extension of the spine, which must be expected with a spinal fixation, but the actions of the spinal ligaments and muscles are not materially interfered with. The range of spinal flexion, extension, and rotation, which you can observe, are quite free and far greater than I had hoped for; in fact, I am pleased to state that the results obtained are far beyond my expectations.

CONCLUSIONS

1. All cases of injury to the spine with deformity and paralysis should have an immediate exploratory laminectomy.

2. Bone transplantation as a treatment for spinal fractures and dislocations offers hope to many unfortunates who are now wearing plaster casts, jackets, or braces.

3. The operation is not a difficult or dangerous procedure, and, when done as a secondary operation, it is not necessary to enter the cord zone in preparing the spinous processes and placing the transplant. A strong bony transplant for an internal splint gives immediate immobilization, extension, and support to the injured spine, which can be secured in no other way.

4. A firm bony union of the transplant to the spinous processes above and below the injury gives the injured spine a firm supporting power almost up to the normal.

5. Should a bony union of the transplant to the spinous process fail, the transplant would give at least a temporary immobilization, support, and extension to the injured spine which could be secured by no other means.

6. Bone transplantation should be resorted to after laminectomy in most cases of fracture and fracture-dislocation of the spine, where the cord is not seriously injured. In the majority of cases it can be done during the laminectomy.

7. It is best to split two spinous processes above and two below the injury, to insure union of the transplant and increase the strength of the spine.

8. The action of the spinal ligaments and muscles are not materially interfered with, so a good range of extension, flexion, and rotation of the spine can be secured.

Before closing, I wish to extend my thanks to Drs. Roy E. Thomas and Willard Smith for their valuable assistance at the two operations. Dr. Roy E. Thomas has had charge of the medical care of the case since the injury and has given valuable assistance and suggestions.

DECORTICATION OF THE LUNG[1]

BY RUSSELL S. FOWLER, M. D., F. A. C. S., BROOKLYN

THIS little girl, two years of age, was first seen by me six months ago with a right-sided empyema. A portion of the rib was resected and the cavity drained in the usual manner. In spite of blow-bottles and gymnastics the lung failed to expand. For this reason pleurectomy is now advocated. In lesions of this character it is much better to cause as near as possible a return to normal — that is, by causing the lung to expand — than to attempt to obliterate the cavity by sinking in the chest wall by a Schede operation. In fact, in the whole line of surgical endeavor those methods are most to be advocated which bring the body to normal or as near normal as possible.

Decortication of the lung was first done by George Ryerson Fowler, October 27, 1893, while Délorme's operation — pleurotomy, with detachment of the visceral layer of the diseased pleura — was performed by Délorme in 1894. As this patient is a child it is extremely desirable that as little blood be lost as is possible; for this reason the chest is opened rather slowly. The incision is made parallel with the ribs with its center at the old drainage opening. The rib at the seat of the old thoracotomy is removed for a space of six inches, the periosteum being left. The opening in the chest is enlarged to introduce the finger, and the cavity is explored. It is found that the cavity extends to the apex of the chest posteriorly on this side; that below, the cavity is bounded by the diaphragm, while internally can be felt the pericardium and lung of the opposite side. The cavity becomes smaller toward the apex of the chest. An incision at right angles to the first is made at its posterior extremity and carried up the chest wall to the third rib. In this case it is not necessary to make an incision in a downward direction as was done in the original decortication operation, though in many cases this original incision is of great use. The arm of the child is carried well over the head, thus raising the scapula out of the way. The flap of soft parts is dissected free from the bony chest wall and retracted upward to the patient's right. As it is retracted, the attachments of the scapula are seen to be quite loose, allowing its ready retraction.

The same subperiosteal resection is now made of each rib in turn, proceeding upward and taking out a little less of each rib as we go upward, as the cavity narrows — six inches of the first, five of the second, and so on. All bleeding points are ligated as fast as they occur. We now have the cavity well marked out and covered only by soft parts, the bony structures having been removed. These soft parts are split directly upward, beginning at the center of the old opening into the cavity and extending the full length of the cavity. As each intercostal artery is cut, it is clamped and ligated. The introduction of retractors on either side of the wound now serves to expose the old empyema cavity completely, so that it can be viewed in all its parts. It is seen that the apex is narrow. Gauze wrung out of warm saline solution is placed where I am not immediately working to conserve body heat.

We have now come to the main part of the operation. This consists in total pleurectomy, the removal of all of the infected membrane which not only binds down the lung and prevents its expansion, but also, from its character, would

[1] Clinical lecture at the German Hospital, March 30, 1914.

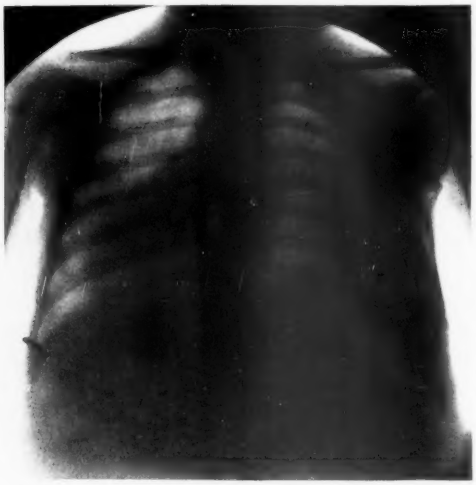


Fig. 1. Showing complete continuity of chest. Lung expanded, filling chest cavity.

continue to cause infection if any of it were left. The incision into this tissue is not begun over the lung itself, for if so done injury to the lung would be hard to avoid; but beginning with the parietal pleura, a start is made and a line of cleavage found which will allow of the stripping of this membrane, not only from the parietes, but also from the lung. This decortication or peeling process is facilitated, after having partly separated the parietal pleura, by catching the edges with clamps; by slight traction on the clamps the peeling process is continued with blunt curved scissors. Only here and there will a snip of the scissors be necessary; for the most part the peeling can be done by blunt dissection. As the lung is approached it is found that the decortication is easier, though here and there little areas of more dense inflammation will render injury to the lung easy. In this case we were particularly fortunate in being able to strip the pleura with comparative ease, the pleura being removed in one broad sheet. This is not always possible: in many cases it is necessary to remove the pleura in strips, and in some cases in which it was found impossible to avoid injury to the lung I have been compelled to abandon the operation temporarily until the visceral injury had healed. Here, as we proceed, we find that the lung has been entered in one place. Failing to close this with a fine catgut suture, a strip of warm saline gauze is held against it while the operation is proceeded with. Again, a little lower down, the lung is injured and the same procedure with warm saline gauze is employed.

It is seen that even in spite of these small injuries the lung is beginning to expand and fill the cavity. The pleura has now been removed in almost its entirety. There remains but a small area of pleura at the apex of the chest wall which, in this case, is almost impossible of removal. With the scissors this surface is scarified and as much of its lining removed as possible. With the two small gauze strips in place against the sites of injury to the lung, the soft parts of the bony chest wall are now replaced and accurately sutured so as to insure the continuity of the ribs which will be reformed by the periosteum which has been left in place. To provide for the large serous discharge which follows this operation, a rolled-up drain of green silk protective is introduced to the apex of the chest on that side and emerges from the original thoracic wound, the edges of this latter being excised. The overlying skin flap is now accuratedly sutured except at the point where the drain emerges.

Addendum. The after-course of this case was interfered with by infection of the wound edges requiring the removal of the stitches on the fourth day. Following the removal of the stitches the flap was strapped in place with adhesive plaster, and finally good primary union was secured. At the time of the removal of the sutures the drainage strip was removed and replaced by a rubber tube at the lower angle of the chest. The X-ray picture (Fig. 1) reveals the continuity of the chest to be complete, showing that the suturing at the time of operation must have been accurate. This picture was taken sixteen days after the operation. The picture also shows the lung expanded and filling the chest cavity.

TRAUMATIC APHASIA

Report of a Case

By H. A. HAUBOLD, M. D., New York City
Surgeon to Harlem Hospital

PRESSURE on a circumscribed portion of the brain, due to trauma, and attended by loss of a special sense, is comparatively rare. We have learned to consider that injury of the cranium sufficiently violent in character to cause paralysis usually also means an increase in the general intracranial pressure which provokes a symptomatology, giving the picture of so-called cerebral compression sequentially manifested by irritation, convulsions, impairment of consciousness, and coma. As a rule, finer distinctions with regard to the localization of solution of continuity of parts and their localization are rendered impracticable, being masked by a rapid impairment of general cerebral function.

"The decompressive operation," so-called, is at best an uncertain quantity when applied to cases where a symptomatology of general cerebral compression follows severe trauma to the cranial contents. Operative effort at relief in severe cases of cerebral compression is a justifiable procedure and is frequently enough followed by successful outcome. Despite the valuable assistance of the radiogram and a careful study of the clinical picture, however, the surgeon approaches with some hesitance the problem of opening the skull in this class of cases in the absence of focal symptoms, which would of course determine the area of attack.

The case reported herewith presented a picture so entirely at variance with that which usually obtains in lesions of the brain due to trauma that it would seem to justify burdening still further the literature with a presentation of a phase of the problem which is distinctive in many regards.

The patient whose case is here recorded was found by the writer walking around the ward in Harlem Hospital. The house surgeon explained that the patient was under arrest, the result of a street brawl. The history recorded on admission (March 25, 1914) described the man as follows:

A. C., Italian laborer, age 41. A small contused wound over occiput, ecchymosis surrounding left eye; slight subconjunctival hæmorrhage at the outer left corneosclerotic junction. Appeared to be aphasic. Pupils equal and reacted to light. Police stated that the man was in a fight three days before admission, but had offered no explanation as to how his injury was received.

The report of the examination made by the house staff showed no abnormality beyond the ecchymosis and the slight scalp wound mentioned above, nor indeed did the examination of the writer elicit other symptoms beyond the fact that the patient made manifest effort to speak. It was clear that the man was not shamming. It was equally clear that he understood what was said to him. His efforts at speech in response to questions both in Italian and English were attended with gesticulation common to his race. He was able to write from dictation in both languages and ultimately his chagrin at his inability to express himself caused him to break down and weep. All other cerebral functions were keenly alert and indeed taking into account the man's unusual physical development, the one lost function stood out in striking constrast.

A radiogram taken by Dr. William H. Stewart (Fig. 1) shows: extending transversely one and one-half inches back from the anterior end of the zygoma a faint translucent line with a slight concavity upwards. Dr. Stewart indicated the fracture by the arrowheads shown in the reproduction of the radiogram. At the time the shadow picture was taken the patient was postured with the left side of the skull toward the film side of the negative. The print of course reverses the attitude.

Dr. Stewart was inclined to believe that the fracture was on the left side of the skull and involved the squamous plate of the temporal bone. The writer does not feel qualified to make fine distinctions in the interpretation of radiograms and from a clinical standpoint the simple existence of fracture of the skull was of great assistance, since in most instances solution of continuity of bone in the cranium due to trauma is very properly regarded as a "bursting fracture" following certain physical laws that are not yet susceptible of application in a given case.

It was regarded certain that deformation of the cranium, the result of fracture, i. e., displacement of fragments, was not the cause of the loss of function, a conclusion warranted by the appearance displayed by the radiogram. In this connection existed the real value of the radiogram.

Fracture of the skull as shown in the illustration was not discovered at the time of the operation, though the area of exposure involved the bone where the fracture was supposed to be. This would seem to indicate that the bone lesion shown was on the side of the skull opposite the traumatized brain area and did not stand in a causative relationship to the aphasia. The writer was inclined to believe that the bone injury (if any) responsible for the clinical picture was located elsewhere and was probably situated at the base of the skull.

Dr. Martin Cohen examined the patient and reported as follows:

March 26, 1914. Examination of fundi: Right disc, color normal. Margin, nasal half slightly indistinct and blurred. Vessels, veins: slightly tortuous. Arteries normal. Left disc, color normal. Margin blurred. Vessels, veins, and arteries normal. Diagnosis: Mild grade of optic neuritis (bilateral). This would seem to indicate an intracranial injury.

Operative effort at relief seemed justified by the motor aphasia, the evidence of fracture as shown by the radiogram, and the ophthalmomicroscopic findings.

Fig. 1. Fracture indicated by arrowheads.

The operative procedure did not deviate materially from that usually employed for the purpose. An omega-shaped flap consisting of scalp and periosteum was fashioned over the speech center on the left side. No fracture was found at this point though this, on the grounds already stated, did not constitute a deterrent with respect to further procedure.

The skull was opened with the Doyen drill and burr and the opening enlarged with the rongeur forceps. The writer preferred this method, in this instance, to the osteoplastic exposure on the ground that it seemed probable that only a restricted area of brain tissue would need to be exposed and that the extent of bone trauma involved in making an osteoplastic flap would perhaps be greater than necessary for the purpose.

The exposed dura did not pulsate. There was no extra dural hæmorrhage found. The total area of exposure was about 1¼ by 1½ inches in size.

When the dura was opened with a crucial incision, about two ounces of thick semifluid blood escaped. A partially coagulated layer of blood was removed from the under surface of the dura corresponding to the third frontal convolution and island of Reil. The brain immediately pulsated synchronously with the ventricular systole; however, blood continued to ooze from the inferior surface of the brain. It is probable that the bleeding came from a torn basal sinus or an unusually large emissary of Santorini, the result of a fracture of the base of the skull.

A slender piece of sterile gauze was carried downward toward where the bleeding seemed to come from, though this did not entirely prevent the oozing of blood. The extracranial portion of the gauze was packed into the opening in the bone and the scalp held in position by interrupted silkworm-gut sutures.

No especial symptoms followed the procedure except that the bleeding during the twenty-four hours following the operation was greater than usually obtains in cases of this sort.

Twenty-four hours later, i. e., forty-eight hours after the operation, the patient was again narcotized and the packing carefully removed.

The bleeding had ceased and the wound was closed in the usual manner.

Up to this time there had been no improvement in the man's speech but the day following removal of the gauze the patient began to speak Italian and could repeat a few words of English.

At this time Dr. Cohen made a second ophthalmic examination with the following result:

Examination of fundi: Right disc, normal in color, margins distinct. Vessels normal. Left disc, normal in color. Margin more distinct than at previous examination. Vessels, veins, and arteries normal. Diagnosis: Distinct improvement in margins of disc in both eyes; i. e., lesion receding.

From this time on the patient made an uninterrupted recovery, reaching about his normal range of speech in both Italian and English in about seven days following the primary operative procedure. If the two days during which the speech area was subjected to gauze pressure be deducted, it may be said that restitution to the normal occurred in about five days.

TRACHEOTOMY; A NEW RETRACTOR AND TUBE PILOT FOR THE EMERGENCY OPERATION [1]

By FRANK LE MOYNE HUPP, A. M., M. D., Wheeling, West Virginia
Surgeon to the Ohio Valley General Hospital

THE tracheotomy tube was used by that capable and daring Byzantine surgeon, Paul of Ægina, A. D. 690; it was used by the medical men at Pompeii, so it is no new story we bring to you to-day. Far be it from the writer to suggest anything which might lead to a complication of the simple methods of this very old operation of opening the windpipe.

Felix Lejars (1) has described tracheotomy as the type of those urgent operations which every practitioner should be prepared to do at any time, in any place, and if necessary with extemporized instruments. Since the advent of the serum treatment of diphtheria, intubation, and upper bronchoscopy, the indications have become much less frequent; but if less often required in cases of diphtheritic laryngitis, it is still urgently necessary for certain injuries, burns, and foreign bodies in the larynx; in œdema of the glottis following extensive phlegmons of the floor of the mouth, the larynx, and the pharynx, or following certain severe types of acute laryngitis, or secondary to cancer of the tongue or tonsil, to retropharyngeal or tonsillar abscess, or to Ludwig's angina or woody phlegmon (Powers), in tuberculosis or cancer of the larynx, in which cases the necessity often arises very suddenly during the course of an unexpected attack of suffocation. Indeed the indications can be summarized in two words: laryngeal asphyxia.

The status of tracheotomy in its relation to obstructive diseases of the upper air passages, particularly croup, before O'Dwyer bequeathed to humanity that priceless legacy, intubation, can best be appreciated when we reflect that of 183,256 cases treated in 150 cities before the combined use of antitoxin and intubation the mortality was 38.4 per cent; whereas the result, since the introduction of serum, is in 132,548 cases, omitting those not treated with serum, a mortality of 9.8 per cent (Rosenthal-Osler). It was the earlier difficulties and surgical tragedies attending the operation of tracheotomy that inspired the inventive genius of O'Dwyer, for when once asked what led to the creation of his tube he replied, "Complete failure with tracheotomy in the New York Foundling Hospital, extending over a period of several years."

The lamented William Kelly Simpson (2), late Professor of Laryngology in the College of Physicians and Surgeons, New York, has said that the horrors and difficulties incident to the operation of tracheotomy in young children, and above all the many fatalities, caused an abhorrence alike on the part of both parent and physician to the extent that the latter gladly delayed surgical interference as long as possible, and in many quarters the operation was practically abandoned and the little ones allowed to die after the gamut of non-surgical methods had been run. Certainly the delay due to this great dread of tracheotomy was itself largely accountable for the fatality attending its performance; for it was a brave surgeon who would tracheotomize in the earliest stages of laryngeal croup.

While it is well known that the real battle of intubation was waged and its glories won before the days of antitoxin, it is also a matter of knowledge that since the discovery of the Klebs-Loeffler bacillus and the introduction of the serum antidote, the tubes of O'Dwyer and the tracheal cannula, so far as their use in membranous croup is concerned, have almost been relegated to the relics of surgical armamentaria.

It seems to be the consensus of opinion among laryngologists that the intubation tube cannot always be depended on. In preparing for the relief of a case of laryngeal asphyxia one should, therefore, always be prepared for tracheotomy (Brewer [3]). An undersized tube may be dropped into the trachea or a piece of diphtheritic membrane or other obstructing substance may be pushed in front of the tube, and thus accentuate the symptoms to the point of suffocation.

Another danger, suggested by Brewer and not infrequently encountered in the operation of intubation necessitating a quick tracheotomy, is the sudden collapse due to the inhibition of the cardiac and respiratory centers, from the irritation of the mucous membrane at the superior aperture of the larynx.

Several years ago, recognizing the high rate of mortality attending the operation of opening the trachea, having personally suffered the experience of two fatalities before the operation was completed, and realizing the imperative need for some retractor and tube guide which might be

[1] Read before the West Virginia State Medical Association at Webster Springs

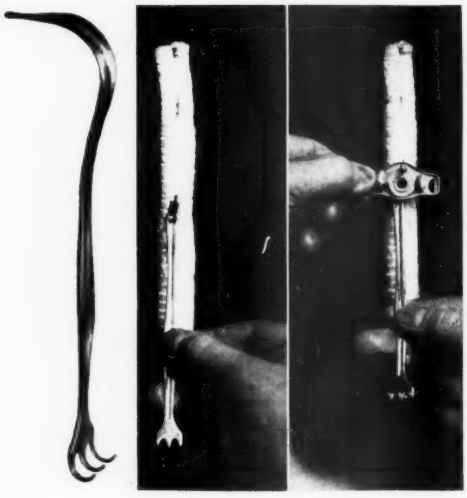


Fig. 1. Fig. 2. Fig. 3.

Fig. 1. Tracheal retractor and tube pilot.
Fig. 2. Showing wide separation of tracheal rings.
Fig. 3. Retractor acting as tube pilot.

quickly and efficiently placed, we devised an instrument for this emergency procedure; and an account of it appeared in the New York Medical Record (4). Our apology for again bringing this instrument to the notice of the profession is that we have modified its form, thus adding materially to its scope of usefulness.

This tube pilot or emergency tracheal-wound retractor is fashioned like a miniature Sims speculum, as may be seen by the photograph, terminating in a probe point, grooved on its convex side like the Sims instrument, but fashioned so that the two sides converge toward the probe point. The retracting device is placed at right angles to the handle, and for convenience we have added a three-prong retractor at the other end of the shaft.

When the tracheal ring or rings have been cautiously divided, it too frequently happens, just as an effort is made to pass the cannula, that the severed rings, either through aspiration or pressure, are inverted, or, perhaps, as we have more than once observed, the cannula has slipped into the cellular tissue, or the imperfectly divided fascia outside of the trachea, and the patient quits breathing. In just such an emergency this probe-pointed guide and tracheal wound dilator may be quickly, but with precision and in a deliberate way, carried along the finger, and forced through blood, if present, into the wind-

Fig. 4. Cannula about to be introduced with the help of the tracheal retractor.

pipe wound. The tracheal incision is now wide open, and with an expulsive cough the asphyxiated patient is relieved.

If there is no tracheal cannula at hand, and no other cutting instrument but a penknife, with the aid of this instrument a patient may be kept alive and comfortable indefinitely until the metal cannula arrives or a cannula may be improvised from rubber tubing, the vital necessity of making an opening into the trachea and letting the air enter at once having been accomplished.

Several cases of urgent dyspnœa due to laryngeal or tracheal stenosis have come under the writer's observation; two were relieved by tracheotomy performed with no other instruments than the emergency retractor and a penknife. Both patients were in the act of suffocating; one from a retropharyngeal abscess, another resulting from laryngeal stenosis due to diphtheria. The third was a case of post-typhoid laryngeal stenosis who had been tracheotomized some weeks before and when the tube was removed there was a return of all the distressing and urgent dyspnœa. In the latter case there was a complicating peritracheal abscess and a mucopurulent bronchorrhœa. Dissection was out of the question: a quick stab was made through the old cicatrix without an anæsthetic and this retractor plunged through the sloughing sinus. Fortunately the trachea was entered, and after the escape of several ounces of yellow, foul-smelling, mucopurulent material, relief was immediate. This case was seen by my colleagues on the staff of the Ohio Valley General Hospital and has since been studied by my friend Dr. Chevalier Jackson of Pittsburgh, and when last heard from he was still wearing a tracheal tube.

To those interested in the subject of chronic obstruction of the larynx and trachea we would refer them to the excellent papers by Dr. John Rogers.[1]

There are cases of the gravest emergency, where suffocation is imminent, cases demanding rapidity of execution, where the trachea must be opened before the bleeding can be arrested.

We have all, as Brewer has described, seen large quantities of blood aspirated into the trachea and bronchi by the first spasmodic respiratory act, causing complete cessation of respiration. Here the sufferer may be resuscitated by the prompt use of the instrument here described, quickly followed by the introduction of a soft rubber catheter to the tracheal bifurcation, with suction, artificial respiration, and wide retraction of the severed rings. The bleeding for the most part from the inferior thyroid vein is quickly relieved the moment air enters the tracheal opening.

There is probably no operation in surgery where hurry, excitement, and fear of death are answerable for so many accidents as in the emergency operation of opening the windpipe. Not one of these accidents should be charged up to the anatomical conditions. Here, certainly, while speed is imperative, a clear brain and a steady hand are likewise indispensable. It is a mistake to say, as Lejars has pointed out, that the operation can be done in a trice; perhaps this is true for operators who have had special experience, or for the internes of a foundling hospital, but for the average practitioner, the operation of opening the windpipe is always a delicate surgical procedure; particularly the emergency operation, whether it be the writhing and blue child with a foreign body or a Klebs-Loeffler membrane, or the fat choking and congested adult. It was with a view of reducing to a minimum this difficulty and the hope of lowering the mortality, after the operation, in these emergency cases that inspired this effort.

GENERAL RULES IN TRACHEOTOMY

1. Local anæsthesia if possible, or combined ether inhalation and local infiltration of novocaine and adrenalin, adopting Crile's assumption that inhalation anæsthesia does not prevent injury impulses from reaching the brain-cells and making them discharge their nervous energy, in a patient already cyanosed to the last degree and all but shocked to death.

2. While the vital necessity is to open the trachea and let in air, remember your anatomy, avoid hurry, be calm, and keep your head.

3. Shoulders raised, head extended and immobilized by the two hands of an assistant.

4. Chin rigid and in line with episternal notch. (Treves [5].)

5. Even retraction from mid-line.

6. Remember that the hæmorrhage from venous engorgement and blocked right heart are relieved the moment the trachea admits air.

7. When suffocation is imminent, be satisfied with touch; do not wait for a sight of the white rings before tracheal incision.

8. While desirable to control bleeding before opening the trachea, delay in accomplishing this may sometimes block the heart and cost a life.

9. Cut cautiously the soft collapsible rings of an infant's trachea; it is but a line or two from the œsophagus.

10. After-treatment of tracheotomized patients is of imperative importance; no case should be left without skilled care. In diphtheritic stenosis the danger time is within forty-eight hours after the exhibition of antitoxin, when the membrane begins to loosen.

CLAIMS FOR THE NEW RETRACTOR

1. Laryngeal asphyxia from any cause may be relieved with this instrument and a penknife.

2. It will guide a cannula quickly, safely, and with accuracy into the trachea, in the presence of copious venous bleeding.

3. In a short, fat neck with suffocating dyspnœa, relief may be given with expedition.

4. It is a useful and safe instrument in the hands of the general practitioner.

5. Where a second operation must be done in the presence of cicatricial tissue and through inflamed tissues, with the aid of the retractor one can enter the windpipe without difficulty.

6. Where the tracheal tube has been coughed out or has slipped for any reason, this retractor is an ideal instrument for a quick and painless replacing of the cannula without anæsthetic or cutting.

We earnestly trust that this little life-saving instrument will give proof of our object in devising it; that is, to lessen the difficulties of others as it has lessened ours, and prevent the tragic ending of some emergency tracheotomies.

BIBLIOGRAPHY

1. Felix Lejars. Urgent Surgery, p. 177.
2. W. K. Simpson. Med. Rec., 1898, March 19.
3. G. E. Brewer. Keen's Surgery, iii, p. 500.
4. Author's paper, "A Tracheal Tube-Guide and Emergency Dilator." N. Y. Med. Rec., July 27, 1895, and Lond. Clin. Notes, 1895, October.
5. Treves' Operative Surgery, xi, p. 188.

[1] Am. J. M. Sc., 1905, Nov.

AN UNUSUAL LACERATION OF THE FEMALE URETHRA

By SIEGFRIED FIGUEROA, M. D., Merida, Mexico

THE following case deserves to be reported, as it was one of a longitudinal laceration, occurring during a miscarriage.

The patient, a woman of Maya Indian descent, forty-seven years old, entered the gynecologic ward of the Hospital O'Horan complaining of incontinence of urine ever since a miscarriage occurring about twelve years ago. Her family history was negative. She had seven normal deliveries, but her eighth pregnancy ended by abortion at the fifth month, being attended during her sickness by a midwife who "extracted the fœtus manually." Shortly afterward and ever since she complained of pain and burning sensation at the vulva and noticed that her urine dribbled out continuously.

Upon examination, I found a thick conical projection of mucous membrane of about an inch in length, hanging down from the distal portion of the anterior vaginal wall, with which it was connected by its broad base. As the accompanying figure clearly shows, it had a vaginal or posterior face and a vestibular or anterior face; at about the upper third of the posterior face there could be made out the vaginal tubercle, and on its anterior face a shallow groove running from its tip to its base could be seen. The vestibular mucosa appeared inflamed and covered by very small papillary projections giving it a velvety appearance. The clitoris was easily located, but one thing was striking, and it was the absence of the urethral opening in its normal location, being occupied by the anterior end of a groove shallower than the one already described and which ran backwards and upwards to meet its posterior end. The angle formed by the meeting of the two grooves was occupied by a small excrescence very much like a urethral caruncle, around which the urine could be seen flowing continuously. With these findings I diagnosed a longitudinal laceration of the urethra and a urethral caruncle. I removed this one and for the laceration I performed a plastic operation.

Case of longitudinal laceration of the female urethra.

This case merits some consideration, as the urethra by its position under the pubic arch and its dense fibrous connections with the surrounding structures is protected from direct violence, at least in its distal extremity, and any undue traction exerted upon it would naturally tend to displace it downward and backward rather than to tear it longitudinally. A dilatation of the urethra would expose it to a tear as the one described by being caught accidentally by the attendant's fingers, and probably this was the etiology of the present case.

SPLENECTOMY FOR PRIMARY PERNICIOUS ANÆMIA

Preliminary Report of two Cases Operated for this Disease

By W. W. ROBLEE, M. D., Riverside, California

CASE 1. W. F. S., a plumber, aged 42. Family history: Mother died at age of 62 of pernicious anæmia; father died at 70 of a cerebral degeneration, the exact nature of which was undetermined. No history of any constitutional disease affecting other members of the family. Personal history good; has not been absent from work more than one or two days at a time for twenty-five years preceding present illness.

Present illness began early in 1913 with progressive weakness, pallor, loss of appetite, and mental depression. I first saw him August 28, 1913; found a pale, depressed, weak individual. He had no appetite, some nausea, and other rather vague symptoms referable to the gastro-intestinal tract. A test meal showed hydrochloric acid somewhat diminished, no blood, cancer débris, or Boas-Oppler bacilli.

Urine normal, both in amount and chemical reaction. Blood: Hæmoglobin, 30 per cent; erythrocites, 2,200,000, with marked poikilocytosis; great variation in size; nucleated reds present; white cells, 6,000, with a normal differential count percentage. Spleen slightly enlarged, lower edge coming to lower costal border. Liver, heart, lungs, and kidneys gave normal findings upon physical examination.

Diagnosis. Primary pernicious anæmia, although cancer of the stomach could not be positively ruled out.

Treatment. Dilute hydrochloric acid internally, atoxyl hypodermatically, and careful forced feeding. He gradually improved, the blood findings approached but never quite reached the normal, and on January 1, 1914, he went back to work. He was not able to put in full time, and on March 1 he was obliged to give up his work again. He grew rapidly worse, and for five weeks before his operation he was confined to his bed. His stomach was very irritable: not only was he unable to eat freely, on account of nausea, but for many months he was very hard to suit dietetically. He was despondent, had given up hope of recovery, and was expecting to die soon. Blood count, May 16, 1,500,000 red cells.

Operation, May 18. Abdomen opened by left rectus incision; stomach, duodenum, and liver found to be free from any growth. Splenectomy under ether anæsthesia — duration 30 minutes. Patient left the table with no evidence of shock. He suffered for two days from nausea, with occasional vomiting spells. From that time on, he gained rapidly in appetite, strength, color, and spirits. Left the hospital on the fifteenth day; walked down stairs and into the automobile easily, and each day since has shown a steady gain. The most noticeable change, aside from the blood picture, was in his digestion and spirits. He began, after the fourth day, to eat freely of everything; his appetite is splendid, he eats many things that he never before enjoyed, and from a notional, hard patient to cook for, he has become a positive delight to his wife, who is a good cook. He has also changed from a despondent, hopeless individual, from whom a smile could not be coaxed, to a cheerful, happy husband and father who feels that he is going to again be of use in the world. No promises of permanent cure were held out to him; he indifferently said to us to do as we pleased when operation was broached, so that his optimism is not based upon any roseate promises made before operation, although the psychical effect of the procedure certainly accounts for much of the mental improvement.

About the middle of June, he began to have colicky pains in the abdomen. These seemed to have their origin in the splenic region. They became gradually more severe and he was again confined to his bed. There was no vomiting or obstipation but the peristaltic tugging could be distinctly observed through the abdominal wall in this region. On July 2d, we opened the abdomen, and found the transverse and splenic flexure of the colon adherent to the abdominal wall at the site of the operation scar. These adhesions were relieved. He had very little discomfort from this work, has been comfortable and steadily gaining since that time. The rich deep red color of the blood at this operation was in marked contrast to the condition observed the first time the abdomen was opened.

Pathologist's Report (Dr. T. R. Griffith): Spleen, 21x12x6 cm.; follicles normal; capsule and trabeculæ somewhat thickened; pigment greatly increased; passive congestion.

Blood Examinations:

May 16, 1914: Red cells, 1,500,000, 30 per cent; hæmoglobin, 40 per cent; color index, 1.4. Stained specimen: Polymorphonuclear leucocytes, 70 per cent; lymphocytes, 28 per cent; eosinophiles, 2 per cent.

There were present normoblasts, megaloblasts, macrocytes, mycrocytes, and a marked poikilocytosis.

May 22: Red cells, 1,164,000 (23 per cent); hæmoglobin, 40 per cent; color index, 1.7.

This examination was made four days after the operation for extirpation of the spleen. The stained specimen showed practically the same picture as in the first examination.

May 26: Red cells, 1,400,000 (28 per cent); leucocytes, 8,000; hæmoglobin, 50 per cent; color index, 1.7.

Stained specimen showed very much less poikilocytosis and the red cells are more uniform in size. There is a marked degeneration of the red cells and a great increase in the number of normoblasts.

June 3: Red cells, 2,000,000 (40 per cent); hæmoglobin, 80 per cent; color index, 2.0.

Stained specimen shows about the same as that of May 26.

June 16: Red cells, 4,000,000 (80 per cent); hæmoglobin, 80 per cent; color index, 1.0.

July 10. Erythrocytes 4,500,000; hæmoglobin, 90 per cent.

Stained specimen: The reds vary much in size, but there are not many oversized cells.

There are large numbers (about 1,000,000 per cmm.) of dwarf-cells, some as small as platelets. These cells are distinct from platelets, of which there were a considerable number, and they stained the same as the normal sized red cells.

Those which were large enough to be properly observed had taken the disc shape characteristic of red cells and some of the cells which were not over two microns in diameter showed a marked poikilocytosis.

There were a number of normoblasts with small well-defined nuclei which took the stain very intensely, but the number of the normoblasts was much smaller than in previous specimens.

There were no megaloblasts observed.

The staining qualities of the red cells were much more uniform, and the fragmentation of the red cells was much less and was confined to the larger cells.

I believe the small cells came from the breaking off of the amœboid processes of the red cells as they were passing into a state of poikilocytosis, the size of the fragment accounting for the size of the cell observed.

The fragmentation of the center of the larger red cells probably was due to a failure of the tissues to furnish soon enough an adequate graveyard for those cells which had outlived their usefulness, in lieu of the spleen which was no longer there to perform its function.

CASE 2. J. B., white, aged 57. Had never been seriously ill; no venereal history. Began to fail during the spring of 1913; was unable to do any work during the autumn and winter, came under my care at the Riverside County Hospital, February 27, 1914. Patient was pale and listless, and complained bitterly of pains in the long bones, especially the tibia. Wasserman test negative; stomach contents showed slight decrease of hydrochloric acid; urine normal. Blood: Hæmoglobin, 65 per cent; erythrocytes, 1,250,000; whites, 6,000.

Operation, May 11, 1914, under ether anæsthesia. Left rectus incision; stomach, duodenum, and liver showed no evidence of disease. Splenectomy, 30 minutes. Patient left the table in good condition and developed no postoperative shock. Began to eat freely on second day and has eaten fairly well since. Has gained in strength and at the end of one month was able to walk up and down stairs and is out of bed the greater part of the day. The improvement in color of cheeks, fingers, and other cutaneous surfaces was very marked within the first week and has slowly improved since. The general improvement was much more pronounced during the first two weeks than it has been since that time. The results so far do not warrant an enthusiastic prognosis, and we are less hopeful of permanent results in this case than we are in Case 1.

Pathologist's Report (Dr. T. R. Griffith): Spleen slightly smaller than normal, measuring 11x7.5x3.75 cm.; pigment increased, otherwise normal appearance.

Blood Examinations:

May 10, 1914: Red cells, 1,250,000 (25 per cent); hæmoglobin, 65 per cent; color index, 2.0.

May 15: Red cells, 1,620,000 (32 per cent); hæmoglobin, 65 per cent; color index, 2.0.

May 19: Red cells, 1,900,000 (38 per cent); leucocytes, 6,000; hæmoglobin, 65 per cent; color index, 1.7.

May 27: Red cells, 1,500,000 (30 per cent); hæmoglobin, 65 per cent; color index, 2.1.

June 24: Red cells, 2,560,000; hæmoglobin, 80 per cent.

July 10. Red cells, 2,880,000; hæmoglobin, 85 per cent.

The stained specimen gave very much the same picture as in Case 1. There were normoblasts, megaloblasts, macrocytes, microcytes, and a marked poikilocytosis.

After the operation there were the same changes presented in the blood as in Case 1. The poikilocytosis became less marked, there were fewer nucleated red cells, less difference in the size of the cells, and there was the same fragmentation of the center of the larger cells. There were no megaloblasts, the nucleated cells being of the normoblast type.

The most marked difference in the two cases was the absence of the minute cells which were so conspicuous in Case 1. The significance of the presence or absence of these small cells is problematical; but from the favorable progress made by Case 1, it might seem to be a favorable symptom to have the small cells present, as it may indicate a more beneficent attempt on the part of the blood-making apparatus to regenerate the blood than in the other case where the cells are apparently of the more mature type.

During the year 1913 an occasional article appeared in the German medical journals advocating removal of the spleen, not only in cases of Banti's disease, but also in cases of primary pernicious anæmia, which had not before that time been considered fit subjects for surgical intervention. These reports have shown that splenectomy, even in individuals who are desperately ill, is entirely feasible and that an immediate and striking improvement results. This disease is one in which great fluctuations in the clinical condition and blood findings are prone to occur. The immediate results in the first few cases might have been explained in this way, but when the published case reports show that all develop this immediate striking improvement, we must conclude that the operative work is responsible therefor. The only case reported in this country is one by Harpole and Fox.[1] The immediate results in that case and in the two cases reported in this article coincide with those reported in Europe. This work is too recent to hazard any opinion as to what the ultimate results will be. So far, the case reports do not show that any patient suffering from this disease, upon whom a splenectomy has been performed, has returned to an entirely normal condition, either as to the blood findings or the physical findings. We are, however, justified in stating that —

First, splenectomy in primary pernicious anæmia, even in those who are very ill, does not present any very unusual difficulties. The operation, unless a former splenitis has been present with resultant adhesions, does not cause much shock or inconvenience to the patient. There has been no operative mortality in the published cases.

Second, the improvement is immediate and striking, and a comfortable, temporary lease of life appears to be assured.

Third, in view of the variability of the conditions in cases suffering from this disease, we are not warranted in promising a permanent cure.

Fourth, the immediate results are far more pronounced than is any palliative operation for cancer or other chronic conditions; and if such an operation is ever justifiable, this operation certainly is indicated. This disease heretofore has been such a hopeless one to combat that any method that can be depended upon to give certain early improvement and which holds out a hope for permanent cure is worthy the serious consideration of all medical and surgical practitioners.

[1]Surg., Gynec. & Obst., 1914, xviii, 243.

A NEW METHOD OF CONTROLLING HÆMORRHAGE FOLLOWING SUPRAPUBIC PROSTATECTOMY [1]

By FRANCIS R. HAGNER, M. D., F. A. C. S., Washington
Professor of Genito-Urinary Surgery, George Washington University; Attending Genito-Urinary Surgeon, Garfield Memorial Hospital and George Washington University Hospital

ALTHOUGH some genito-urinary surgeons whose opinion I respect greatly consider that it is not necessary to use any means to control hæmorrhage after a suprapubic prostatectomy, I know there are others who feel just as strongly that it *is* necessary to use something to control bleeding. We know these patients are old, and many are in such a debilitated condition that I cannot help but feel that our mortality records will be lower if we use some method to control this hæmorrhage.

It is not necessary that the patient should bleed to death for the hæmorrhage to be harmful. Old, debilitated men losing blood over several hours thus lowering their resistance have less chance to recover. Furthermore, my own peace of mind is to be considered, for if I have my pneumatic bag in the patient I am sure that he is not going to bleed.

Pneumatic pressure is not a new idea, as it has been employed before. We know that for years an ordinary condom inflated with air was employed as a pressure agent to check nasal hæmorrhage. We have used various forms of packing in prostatectomy cases, and until the advent of this little pneumatic bag we had used an arrangement of gauze and catheter, similar to that used by Dr. Lower of Cleveland.

Disadvantages. The troubles with gauze in controlling hæmorrhage are (1) that it does not always control it, necessitating repacking; (2) that pain is often caused in its removal; and (3) that secondary hæmorrhage may be produced by removal of the gauze, although this is infrequent.

This little bag overcomes all these obstacles and is a great time-saver. I believe it is more comfortable to the patient than the pressure of gauze packing.

We tried this bag first on March 3, 1914. We have used it on ten patients, only one complaining of the presence of the tube in the urethra; this man had an exceptionally tender urethra.

You will see from the drawing that the tendency of this bag, when in place, is to accomplish what Dr. Lower of Cleveland and Dr. Walker of Baltimore have felt necessary; namely, the pushing of the capsule inwards toward the urethra—not to fill up the cavity and push it back into the bladder.

The bag, made of rubber, is constructed so as to fold automatically when deflated (see cut). A rubber tube is attached to the open end of the bag. To the other pole of the bag is attached a small rubber loop to which a string is tied to facilitate its removal through the suprapubic wound. We have also had made a bag with an inlet and outlet tube so that it may be distended with hot or cold water; but the simpler bag controls the hæmorrhage so perfectly that we have found the more complicated bag unnecessary.

The following is the method of application: A specially constructed sound with beveled end (see cut) is passed into the urethra and out through the suprapubic wound; the tube attached to the bag is threaded over the beveled end and the sound withdrawn through urethra, the tubing being pulled through and the bag pulled into place by traction on the tube. The bag is then distended with air by Janet's syringe, the pressure within the bag being readily discernible by the back pressure on the syringe. It is well to pass the finger into the bladder through the suprapubic wound and sweep it around the bag where it comes in contact with the orifice of the urethra,

Sound for drawing tube through urethra.

Bag deflated.

[1] Read before the American Association of Genito-Urinary Surgeons at Stockbridge, Mass., May 16, 1914.

Bag inflated.

to insure its being in proper position. This also adjusts the mucous membrane at the urethral margin. The air is retained in the bag by clamping or tying the tube that remains outside the urethra.

To help hold the bag in place, we have wrapped gauze around the tube where it comes in contact with the end of the penis; however, the cut-off muscle tends to shut down on the tube and hold the bag in position.

In the ten prostatectomies above referred to, there had been no filling of the bladder with clots; if continuous irrigation is used, the fluid will come away clear, the bag may be put in place, and bladder irrigation will show a good deal of blood escaping; but just as soon as the bag is blown up and pulled into place, this hæmorrhage ceases immediately. These patients are all recovering, or have recovered, from the operation.

In one case the action of the bag was quite striking: The man was in a very precarious condition, having had serious hæmorrhage from the prostate before operation. The prostate was very large and appeared very vascular; the hæmorrhage was great, the pulse going from 90 to 150 in the 5 minutes required to remove the gland. When the bag was put in place the blood was flowing rapidly from the suprapubic wound; as soon as the bag was put in position, the active hæmorrhage ceased, and after the clots were washed out the irrigation returned not even blood-tinged. Dr. Squier, of New York, has used this bag on one case and informed me that the hæmorrhage stopped immediately following the drawing of the bag into position. At the end of twenty-four hours we have let the air out of the tube, and at the end of forty-eight hours the bag has been removed; in one case the air was let out in twelve hours and the bag removed at the end of twenty-four hours.

It may be necessary to keep the bag distended only a few hours, after which if hæmorrhage should recur it would be very simple for an assistant to blow up the bag and pull it into position.

The removal of this bag is accomplished without inconvenience to the patient, quite in contrast to the removal of gauze. Suction is made on tube to insure complete closure of bag before its removal; the urethra alongside of tube is irrigated with boric acid; the tube hanging out of urethra is carefully washed with soap and water, followed by bichloride solution and sterile water. Oil is injected into the urethra and the tube outside the urethra is well anointed with sterile vaseline; traction is now made on the string that is attached to loop of the bag, the tube hanging out of urethra is fed into the urethra as is a catheter, and the bag is removed through the suprapubic wound.

A MODIFICATION OF THE TECHNIQUE IN THE OPERATION FOR SUPPURATIVE APPENDICITIS, BASED ON POST-OPERATIVE HÆMORRHAGE

By CHARLES STANLEY WHITE, M. D., Washington
Associate Professor of Surgery, George Washington University

THE following case is a type of which there are many and serves to illustrate the object of this paper:

R. D., age 41 years, was seen November 13, 1912, in an acute attack of appendicitis of a few days' standing. He was operated the same afternoon, the rectus incision being made, expecting to close without drainage, but the necrotic appendix precluded such a technique and a rubber tube was inserted. On the fourth night after the operation the nurse reported the dressings saturated with fresh blood and a sharp rise of the pulse, 88 to 120. During the next twenty-four hours the dressings showed considerable fresh hæmorrhage, notwithstanding the wound was firmly packed about the tube. Salt solution was used by rectum and a large amount of water given for the inordinate thirst. The hæmorrhage did not recur after the fifth day, and aside from a slight purulent discharge, the convalescence was good.

It is the opinion of the author that the source of the hæmorrhage was the deep epigastric artery, which was eroded by the drainage tube or opened by an advancing infection. Hæmorrhage from this artery has been fatal in a few cases, and why more do not occur is remarkable, for it is not uncommon to see this vessel with its companion veins exposed in drainage cases of appendicitis. It is probable that a thrombosis occurs in the zone of intense infection; but at the best, this is an unreliable means of meeting the possibilities.

During the past year we have anticipated this accident by ligation of the artery and veins in the lower end of the incision, using two ligatures about an inch apart. In the early cases we cut between, but recently we have abandoned this step. We can expect a clot to form, not only between the ligatures, but above and below the distal and proximal ligatures respectively. The free anastomosis that this artery possesses, especially with the internal mammary, assures a good vascularization of the contiguous structures.

We believe the routine ligation of the deep epigastric in drainage cases when the incision approaches the vessel will reduce the morbidity and mortality of the surgical treatment of appendicitis.

A CONTRIBUTION TO THE DISCUSSION ON "THE RESULTS OF OPERATION (LARYNGOFISSURE) FOR INTRINSIC CANCER OF THE LARYNX"[1]

By SIR ST. CLAIR THOMSON, London, England

TO the English members of this Congress Professor Schmiegelow's paper must have produced two different emotions; the first emotion is that of gratitude and satisfaction at his very handsome recognition of the fact that the pioneers in this subject were British laryngologists and that it is to Sir Felix Semon and to the late Sir Henry Butlin that mankind is in the first instance indebted for the establishment of an operation which saves more lives from death by cancer than does any operation on cancer in any other part of the body. The second emotion is surely one of surprise that Professor Schmiegelow from a smaller country with a vastly smaller population is able to give the records of a much larger number of cases than any single surgeon can produce in this country where the operation may be said to have been founded. Is it with laryngofissure as it was with the work of Bodington and the treatment of tuberculosis, and as it was with Lister and the re-creation of surgery, and as it was with the discovery of aniline dyes? It really looks as if every piece of original work in Britain had to go abroad and be born again before being generally accepted in the land of its birth. Or, is it because both the profession

[1] Presented in the discussion of Professor Schmiegelow's paper on "The Results of Operation (Laryngofissure) for Intrinsic Cancer of the Larynx." See Surgery, Gynecology and Obstetrics, September, 1914, p. 339.

and the public in Denmark are better instructed and more alive to the progress of medicine that Professor Schmiegelow can record 33 cases, when, with unique opportunities, Semon's full score was 24, and my own, so far, is 17. If so, a similar explanation would apply to South Germany, where Killian from the small provincial town of Freiburg was able to publish a larger number of foreign bodies extracted from the air-passages and gullet than any single laryngologist can do in the large cities of this empire. Now that the work initiated in London has been so successfully carried forward on the continent and in America and has been so handsomely appreciated by Professor Schmiegelow this evening, let us hope that in England more patients will present themselves in time and that their medical advisers will recognize what can be done for them. Professor Schmiegelow's statistics agree with those of Semon in this country, and of Chevalier Jackson in America, in showing that cancer of the larynx in the majority of cases is situated on the vocal cords. Hence, the most evident and constant symptom is a change in the voice. No individual should be hoarse more than three weeks without at least securing an inspection of his larynx and a skilled opinion as to the condition of his vocal cords.

I am not sure whether in the ten minutes at my disposal I am expected to act as an *advocatus diaboli* and attempt to dissect the excellent paper we have heard; but if so I have very little to say. I am in complete accord with Professor Schmiegelow in the employment of a general anæsthetic, in doing a tracheotomy, in removing the tracheotomy tube before the patient leaves the operating table, and in getting the patient out of bed as soon as possible.

His death rate from operation is somewhat heavier than that of Sir Felix Semon, or of myself. Semon had only one death from operation among 24 cases and that was evidently due to the administration of ether per rectum, a dangerous proceeding which I regret to say there is some effort to revive. I have done laryngofissure 17 times for intrinsic cancer of the larynx without a single death. I understand that the deaths in Professor Schmiegelow's statistics occurred among his earlier cases when he used to employ plugging of the larynx. Time does not permit of considering the technique in detail, but I cannot refrain from mentioning that I am well satisfied with the administration of chloroform by the mouth; the avoidance of Hahn's tampon cannula or any such contrivance; with allowing the patient to sit up in bed as soon as ever he recovers consciousness; with freely open windows and the avoidance of steam-tents or similar asphyxiants; and finally, with getting him out of bed and eating solid food within 24 to 48 hours.

As to recurrences, Schmiegelow records 11 in the 28 patients who survived the operation, or 40 per cent; Semon in 24 cases had 3 recurrences or 12 per cent. In 17 cases I have had two recurrences or about the same percentage; but if I take only the 13 cases who have passed the one-year limit established by Semon, my percentage of recurrences would be 15 per cent.

To conclude, I would here briefly record my own statistics:

Cases of intrinsic cancer of larynx treated by laryngofissure	17
Deaths from operation	nil
Died from recurrence	2
Recurrence, laryngectomy, and alive 4½ years later	1
No recurrence, including the last mentioned case.	15
Dead from other causes 15 months, 3 years, 4 years, and 11 years after operation	4
Alive, 7 years after	1
Alive, 5½ years after	1
Alive, 4¾ years after	1
Alive, 3¾ years after	2
Alive, 2 years after	1
Alive, 1¾ years after	1
Alive, 9 months after	1
Alive, 8 months after	1
Alive, 9 weeks after	1
Alive, 5 weeks after	1

In no case did thyrotomy reveal any error of diagnosis although a preliminary microscopic examination of a removed portion was only available in six instances.

General anæsthesia was used in all but one case.

One case died from separate and unconnected development of cancer in another part of the body.

Laryngofissure is not, in skilled hands, a dangerous operation. It shows far better results than the operations for cancer in any other part of the body; and for intrinsic cancer of the larynx, treatment by laryngofissure is the only way.

BOOK REVIEWS

A CRITIQUE OF NEW BOOKS IN GYNECOLOGY AND OBSTETRICS

By GEORGE GELLHORN, M. D., Saint Louis, Missouri

A MEDICAL work of almost eight hundred pages which within five years reappears in a third edition carries its own credentials. In the case of Bandler's Medical Gynecology, it should be added that this book strikes a note which is fast becoming the dominant one in our newer conceptions of therapeutics. Gynecology has expanded beyond its original scope of merely treating the diseases and injuries of the pelvic organs as such. Modern gynecology takes a wider outlook and considers the normal and pathologic genital functions in their relation to the general physical and psychic health of woman. In carrying out, in detail, this principle of dealing with gynecologic diseases, Bandler's book represents the new science of pathologic physiology and must needs appeal strongly to the general practitioner as well as the gynecologic specialist.

Bandler's attitude becomes at once apparent by a glance at the headings of some of the chapters. He devotes 58 pages to a discussion of the internal secretions and gives us, in a very concise form, an excellent exposé of this important and interesting field which has just been opened to medical research and which bids fair to revolutionize many of our therapeutic methods.

The chapters on "Amenorrhœa" and "Dysmenorrhœa" are exceptionally clear and exhaustive, and here as with all other subjects the effects of extragenital factors are lucidly set forth, and constant allusion is made to the etiologic and therapeutic importance of the glands of internal secretion.

The most frequent symptoms of gynecologic patients, leucorrhœa, uterine bleeding, and pain, notably backache, are dealt with in separate chapters. For senile vaginitis Bandler recommends pyroligneous acid, which in the reviewer's experience, acts as a specific and deserves wider application in the hands of the practitioner.

The chapter on "Associated Nervous Conditions in Gynecology" deserves careful study. Nervous symptoms at puberty, in chlorosis, during menstruation, and in pregnancy are discussed. Attention is called to masturbation as a cause of nervous disturbances, and the relation of ptoses to neurasthenic symptoms is fully considered. Cardiac phenomena associated with sex factors, hyperthyroidism, hypophysis disease, and the climacterium as a source of nervous symptoms are given due consideration. Hysteria is a diagnosis made too frequently where there is in reality neurasthenia present, and in this view most gynecologists and neurologists will concur. The diagnosis "reflex neurosis" should be made with great care. Too often it cloaks ignorance or hasty conclusions. Rarely do pelvic abnormalities cause pain elsewhere through "reflex" unless there exists a hysterical predisposition. The author maintains, that a thorough examination will often show general conditions outside of the genital sphere or even the unfavorable influence of modern culture and social conditions responsible for many annoyances erroneously attributed to uterine malpositions, to cervical lacerations, etc.

The chapter on "Constipation," written by Dr. George Mannheimer, is characterized by the same wide outlook typical of the other sections of the book. The treatment of constipation must dispense with the pernicious drug habit; it consists of hygienic, dietetic, and mechanical methods, and, where they can be ascertained, demands the removal of etiologic factors.

The remaining chapters take up the various diseases of the generative organs, and show in each instance how much can be accomplished by non-operative means. This by no means implies that there is a sharp line between operative and medical gynecology. To delegate to the surgeon one part of gynecologic therapy (as is still the prevailing fashion) and to another man the non-operative part, is obviously illogical and contrary to the best interests of the patient. Numerous conditions should be treated surgically only after a preliminary non-operative treatment; and conversely, many operations can benefit the patient only when supplemented by conservative means. Only thus shall we arrive at the true conception of gynecology as a speciality.

The chapter on "Methods in Medical Treatment" enumerates applications to urethra, bladder, vulvovaginal and urethral glands, vagina and uterine cavity. The oft-repeated teaching that, in intrauterine treatment, the cervix and especially the internal os must be wide enough to permit of thorough drainage is too often ignored. Bandler is an advocate of atmocausis and devotes considerable space to the discussion of this procedure, without,

Medical Gynecology. Third Edition, thoroughly revised. By Samuel Wyllis Bandler, Philadelphia and London: W. B. Saunders Company, 1914.

however, convincing us that this method with its complicated technique and numerous dangers could not well be replaced by other and simpler means. In reducing a retroflexed uterus he employs solely the bimanual method, but in our experience this will often fail, where Kuestner's method or the use of a mercury colpeurynter will succeed. The treatment of vaginal discharges by means of drying powders is only briefly mentioned. This method, inaugurated by Nassauer of Munich, has so many advantages that it deserves more detailed discussion in the next edition. The same is true of the application of dry heat for the production of pelvic hyperæmia, and the acetone treatment for inoperable cancer of the cervix. The latter, in particular, efficacious as it is, recommends itself for general use because it is easily applied and quite painless and possesses undoubted advantages over the thermocauterization advised by Bandler.

These and a few other technical points, in which one might differ from the author's suggestions, cannot detract from the value of the book as a whole. The principles enunciated in this volume are bound to meet with universal approval, and the gynecologist who makes these principles his own will not lay himself open to the satirical accusation that "he looked upon the world in general and his patients in particular through a vaginal speculum."

GOETHE'S dying sigh "Mehr Licht" seems particularly applicable to the field of sexual hygiene, where utter darkness has reigned so long. We are all agreed that sex instruction is necessary, and most of us are also agreed that such instruction comes best from the parents. But most parents have as yet distorted views on the subject themselves and are woefully ignorant on many points; or else they are still "ashamed" to speak to their children of that fundamental instinct to which they owe their own existence and the lives of their children — so that in this stage of transition, the physicians are the natural teachers for old and young and the best preachers of the gospel of Knowledge versus Ignorance.

There is no dearth of literary productions from the pens of medical men dealing with the sex problem, but many of the books offered will be found wanting on closer scrutiny. Some are too technical, others too sentimental, and there are also some that parade under the cloak of popular scientific communications which in reality should be classified as obscene literature.

It is, then, a pleasure to read, and recommend to others to read, two small volumes which have recently appeared in print. They represent in an amplified form a series of lectures rendered by Dr. Steinhardt before a number of educational societies and other clubs. These "sex talks" are meant for "girls 14 years and older" and "boys 10 years and older" respectively, but first of all they should be carefully read and reread by parents. The subject matter, as given in these books, suggests itself: the anatomy and physiology of the genital organs, the significance and hygiene of puberty, masturbation and coition, moral and physical cleanliness, the effects of venereal diseases upon the present and the coming generations, etc. The salient point remains this: *how* to say all these things; and the author has solved his rather difficult task in a most successful fashion. He is simple and direct and he speaks with such sincerity that an atmosphere of confidence, is at once created between him and his readers. Even if here and there some of the anatomical and physiological details are above the heads of the average lay reader, yet the author drives his lesson home that the wage of ignorance is untold suffering. "Forwarned is forearmed" is his motto, and these two little volumes are valuable factors in the mighty movement toward enlightenment of the masses.

TEN SEX TALKS TO GIRLS (14 YEARS AND OLDER). By Irving David Steinhardt, M. D. Philadelphia and London: J. B. Lippincott Company, 1914.

TEN SEX TALKS TO BOYS (10 YEARS AND OLDER). By Irving David Steinhardt, M. D. Philadelphia and London: J. B. Lippincott Company, 1914.